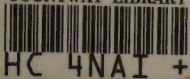


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March 1929

THE CLIMACTERIC

(THE CRITICAL AGE)

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(THE CRITICAL AGE)

BY

GREGORIO MARANON

PROFESSOR OF MEDICAL PATHOLOGY IN THE MADRID GENERAL HOSPITAL, MEMBER
OF THE ROYAL NATIONAL ACADEMY OF MEDICINE

TRANSLATED BY

K. S. STEVENS

EDITED BY

CAREY CULBERTSON, A.B., M.D., F.A.C.S.

ASSOCIATE CLINICAL PROFESSOR OF OBSTETRICS AND GYNECOLOGY, RUSH MEDICAL
COLLEGE OF THE UNIVERSITY OF CHICAGO; ATTENDING OBSTETRICIAN AND
GYNECOLOGIST, PRESBYTERIAN HOSPITAL; CHIEF OF THE GYNeco-
LOGICAL STAFF, COOK COUNTY HOSPITAL; FELLOW, AMERICAN
GYNECOLOGICAL SOCIETY AND CHICAGO GYNECOLOGICAL
SOCIETY; MEMBER, CHICAGO PATHOLOGICAL
SOCIETY

ST. LOUIS

THE C. V. MOSBY COMPANY

1929

of man himself. The study of the psychology of animals has doubtless contributed vastly to the knowledge of the human mind, but were we limited to this material, we should know no more than the giant trees do concerning the intelligence of the lord of creation. The same thing is true of the pathology of man, and particularly in those branches of pathology remote from the purely vegetative.

That part of our endocrine knowledge which has no experimental origin but only a clinical one, and is perhaps contrary to experimentation, is as legitimate for us as that which the laboratories have provided. And to all this should be added the hypotheses necessary to fill in the gaps which the meagerness of our knowledge leaves between truths. To insist that hypothesis may be as necessary to the progress of science as truth itself appears absurd, but it is not, provided, of course, it is supported by concrete facts. The best way to cross a river is by a wide bridge, but when this is lacking and it is necessary to reach the other side one may leap across by way of the rocks which protrude from the waters sufficiently to bear the foot and provide new impetus. The danger is in confusing hypotheses with evident truths, but that is the error of a beginner, of whom there is no need to speak.

The present edition is translated from the second Spanish one, which appeared in 1925. For this reason some notes and bibliographic data have been added with the aim of bringing the material up to date.

It remains for me to extend my thanks to the translator, K. S. Stevens, and to Dr. Carey Culbertson who has revised and annotated the text, to Dr. Mabel Matthies for her kind assistance with certain portions of the translation, and to The C. V. Mosby Company, of St. Louis.

G. Marañón.

Madrid, 1927. .

PREFACE TO THE SECOND EDITION

I make no attempt to conceal the fact that of all my books I feel a particular affection for this one, now going into its second edition. In the life of man, as in that of nations, the study of an epoch, of an age, infinitely surpasses in interest the study of isolated facts. When these facts are grouped and considered as part of a period in the general evolution, they take on a new consequence and live. Then they explain and complete one another. They appear no longer as so many "museum pieces" displayed under artificial light, which is the impression given by independent descriptions of these same facts.

Despite the circumstance that the present scientific mode—most prejudicial and odious—began, some time ago, to swing away from the tendency toward giving an excessive influence to sexual life in the affairs of human beings, I am daily more and more convinced that this influence reaches to the remotest corners of human life. Doubtless the instinct for self-preservation reigns as co-tyrant with the sexual instinct. But by this I do not mean that they are mutually exclusive. On the contrary, in their deepest roots these two forces are as inseparable as are those of the individual and the species. When man is actuated by the instinct of self-preservation he also bows to the species and therefore obeys a mandate which is remotely sexual. Inversely, every sexual act contains within itself a force of egoism impossible to separate from the instinct of self-preservation. The error lies in confounding the sexual instinct with libido, that is, with the instinctive force which impels the male toward the female. The sexual instinct has its moment of expression culminating in libido, but the instinct itself is far more extensive. In this book I attempt to demonstrate to what remote and quiet regions its limits reach. It is indubitable that libido, pure or transformed, controls a goodly number of human acts and feelings. And it is also certain that many more, perhaps the majority of our acts and feelings, remain perforce within its zone of influence. But there are no books on the

sexual influence in this other circle, the largest and most interesting, which we may call extralibidinous. The material found in climacteric humanity is particularly propitious for the study of this great problem. Hence a consideration of sexual psychology occupies a great part of this book, aside from the purely gynecologic and medical matters.

This second edition of my *Critical Age* has been completely revised. Thus it may be said that only the general structure and the unchangeable facts remain. A large part of the doctrine pertaining to the internal secretions has been recast. Many new facts recognized by myself or my coworkers have been added. In short it is no exaggeration to say that, with the exception of a few isolated pages, this is a book which has been carefully pondered and wholly rewritten.

G. Marañón.

Madrid, Toledo, 1925.

PREFACE TO THE FIRST EDITION

In considering the menopause we face a curious fact. The newly graduated physician has scarcely more than a vague idea of what this state is and what it signifies in human physiology and pathology. If he turns to the literature for an amplification of his vague, general idea, he will have a hard time finding a comprehensive and modern study of the climacteric transition; but he will find more literature on almost any rare disease, which will, perhaps, not be presented once in a whole life time of medical practice, than on menopausal physiopathology. Yet the problem of the menopause comes up every day, every hour, in the professional work of every physician. And he must decide without previous pathogenetic criterion to guide him, whether this or that phenomenon presented in the critical years, or this or that form acquired by an existing disease on reaching this period, is a pure coincidence or may be directly related to the crisis as its cause.

These facts impelled me to study this subject with especial care, clinically and, as far as possible, experimentally. The

recent studies on the internal secretions, illuminating as they do obscure areas of the pathogenicity of the menopause, have enabled me to orient the problem in a new way. In this book I have attempted to give my new point of view and that new point of view constitutes the book's sole and rather modest merit. What I have to say—in actual facts as old as humanity—turns, as on an axis around this matter. The menopause is not merely a syndrome of genital insufficiency, as was thought until recently, but is the biologic consequence of a complex and constant endocrine crisis, like that of puberty, the glandular elements of which can be made out with some claim to exactness. This greater knowledge of the mechanism of the crisis enables us to interpret clearly and to treat correctly many details of climacteric phenomenology which hitherto were obscure. From this point of view, the classic concept of the *menopause* as a simple genital incident in woman disappears. In its place, appears the much more comprehensive concept of the *critical age*, that is, of a long period of life in either sex, the nucleus of which is the genital subsidence, but in the development of which all organic activities participate.

Apart from these reasons of didactic order, I believe that for the medical observer this period of life is without doubt the most interesting. In it the vegetative and psychic activities have acquired their maximum powers and the functional completeness and serenity which experience gives. The beginning of the decline shows itself, in each one of these activities then in apogee, by a state of *erethrism* and instability which is very characteristic and striking. The circulatory system, nervous system, and nutritive metabolism are exquisitely sensitized. This permits them to deviate, on minor stimuli, from the normal. The same thing occurs in the emotional life, which becomes extremely sensitive. The critical age and emotion are united by indubitable and suggestive physiologic links, as I shall attempt to demonstrate. This is true up to the point where this age may be called with nice exactness the *age of emotion*. All these general characteristics of the climacteric period are the reflection of a parallel state of functional irritability in the endocrino-vegetative system which precedes the phase of frankly senile decline.

All these considerations led me to prepare this book. I have conceived it from the general practitioner's point of view and for all physicians. That is, I have not looked at the subject from the narrow perspective along which gynecologists, the ones chiefly concerned with this subject, have been accustomed to regard the problems of feminine pathology.

I have tried to express as concretely as possible what I have to say, since I am convinced that the day of large volumes is definitely past. It seems to me that some subjects are still treated at excessive length, and others, on the contrary, with excessive brevity. I prefer to err on the side of brevity. I have included only those clinical histories necessary to give that atmosphere of reality which I believe indispensable to these studies. The bibliography, which I fear is too long, has been kept down to the really essential citations, but even so they exceed 300.

G. Marañón.

Hernani, 1918, Madrid, 1919.

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THE CLIMACTERIC

CHAPTER I

PLURIGLANDULAR THEORY OF THE MENOPAUSAL CRISIS

Climacteric and Menopause

Before beginning this study, the concept and terminology of the *menopause* and of the *climacteric*, or critical age, must be explained. Although obviously distinct, these terms are confounded with excessive frequency in ordinary professional and common speech. The *menopause* is an isolated phenomenon, the *physiologic cessation of the menstrual flow*. The *critical age*, or *climacteric*, is a period of life characterized by a complexity of phenomena, the central symptom of which is precisely this menstrual cessation, but which is accompanied by many other disturbances such as those of a circulatory and nervous nature. This fundamental difference, then, must not be forgotten even when the term "menopause" is loosely used giving it an undue latitude. I shall refer to this differentiation in terms from time to time.

Endocrine Crisis of the Menopause

Once this point is clear as to the distinction between the menopause and the climacteric, or critical age, we may pass at once to the *pathogenetic study* of the climacteric. This period of life has been discussed by physicians since the time of Hippocrates. Whether the reader will find much that is new and suggestive in the present volume will depend upon his ability to look at the subject from a new point of view, one which differs radically from that held by earlier writers.

Here is my thesis for demonstration: *The pathogenetic mechanism of climacteric symptomatology is not limited to insufficiency of the genital gland, as has been held, but it is rather the expres-*

sion of a complex endocrine crisis, which varies in different individuals. In this crisis the outstanding feature is gonadal insufficiency to be sure, but other glandular disturbances occur coincidentally and form an essential part of the crisis. Our knowledge concerning some of these various glandular disturbances is now fairly well established.

Furthermore, it is now evident that the endocrine is not the only upset in this menopausal crisis. Any organ or system in the body may share in the complex symptomatology of the climacteric. Some do so almost constantly, particularly the circulatory and the nervous systems, while such others as the digestive or respiratory tracts share less frequently. But the endocrine reorganization due to ovarian insufficiency plus the pluriglandular reaction which this establishes is the directing pathogenetic element. It is analogous to the pubescent crisis with its sudden activation of the genital function, previously latent, plus a pluriglandular reaction. On the basis of this disturbance of the endocrine system, it becomes easy to interpret those symptoms which formerly appeared to be disconnected as really comprising a combination which in its entirety forms the climacteric. Thus certain symptoms may be linked to disturbances of this or that particular gland. Other symptoms are obviously influenced by endocrine imbalance. And in endocrine data we shall find a useful point of reference in interpreting those symptoms the pathogenesis of which lies wholly outside the glandular system.

It is now twelve years since I first advanced this *pluriglandular interpretation* of the critical age.¹ In subsequent publications^{2, 3} my ideas were developed at greater length. In the first edition of this book I expressed myself with rather marked effusion, but I have no regrets, as that enthusiasm was sincere and the result of the newness of the idea and of my youth. All the episodes of sexual life are now considered "complex endocrine crises." And this concept is doubtless one of the great contributions of endocrinology to biology within the last twenty years.

¹Marañón: *La doctrina de las secreciones internas*, Madrid, Corona, 1915.

²Marañón: *Algunos puntos poco conocidos de las secreciones internas*, Lectures at the Biological Society of Barcelona, April, 1917.

³Patogenia de la menopausia, Conference at the University of Saragosa, April, 1917.

General History and Bibliography

The literature on the menopause in its relation to the internal secretions is still relatively small. Although the internal secretion of the ovary has been well studied, and from the first the disappearance of this secretion has been recognized as beyond doubt the main factor in climacteric pathogenesis and symptomatology, yet there are only a few texts wherein the menopause is studied as a case in particular of ovarian insufficiency. In the French literature of the last fifteen years we find various important works oriented from this point of view, such as the theses of Thiercelin,⁴ Le Barzic,⁵ Levi,⁶ Darcanne-Mouroux,⁷ Alaize,⁸ Jardry,⁹ Drevel,¹⁰ Villemin,¹¹ among others, and above all Vinay's monograph, *The Menopause*,¹² which begins with an excellent study of ovarian insufficiency.

In German literature, on the contrary, no such idea is upheld. The most prominent writer on these subjects, Kisch, even in the second edition of his interesting work, *The Sexual Life of Woman*,¹³ makes no allusion to ovarian function or to ovarian therapy in the study of the menopause. Not even in Schickele¹⁴ do we find a treatise in an endocrine sense, on the critical age. Even in the recent and voluminous works on endocrinology by Biedl,¹⁵ Falta,¹⁶ and Pende,¹⁷ there is but scant allusion to the

⁴Thiercelin: Contribution a l'étude de l'opothérapie ovarienne, Paris, 1898.

⁵Le Barzic: Traitement des troubles de la ménopause naturelle par l'opothérapie ovarienne, Paris, 1899.

⁶Levi: Les bouffées de chaleur de la ménopause opératoire, Paris, 1900.

⁷Darcanne-Mouroux: La ménopause précoce, Paris, 1904.

⁸Alaize: Le rôle de la fonction interne de l'ovaire, en pathologie nerveuse et mentale, Montpellier thesis 1906.

⁹Jardry: La sécrétion interne de l'ovaire, Paris, 1907.

¹⁰Drevel: Effets thérapeutiques du corps jaune de l'ovaire, Paris, 1907.

¹¹Villemin: Le corps jaune considéré comme glande à sécrétion interne de l'ovaire, Paris, 1908. In this interesting thesis is found a good résumé of the question concerning the value of the corpus luteum as a gland of internal secretion; also a large bibliography.

¹²Vinay: La Ménopause, Paris (without date). This is a clear summary of the menopausal problems. Many of the chapters are copied, however, from other French works, such as that of Barbaud and Rouillard on which comment will be made later.

¹³Kisch: The Sexual Life of Woman. English edition, 1910, Rebman Company, New York.

¹⁴Schickele: Die nervösen Ausfallserscheinungen der normalen und frühzeitigen Menopause in ihren Beziehungen zur inneren Sekretion, in Handbuch der Neurologie by Lewandowsky. Bd. IV, Berlin, 1913.

¹⁵Biedl: Innere Sekretion. Fourth edition, Berlin, Wien, 1922.

¹⁶Falta: Die Erkrankungen der Blutdrüsen, Berlin, 1913. Falta; Endocrine Diseases, ed. 3. Philadelphia. P. Blakiston's Son and Co.

¹⁷Pende: Endocrinologia, ed. 2, Milan, 1920. Of the large works on Endocrinology, this gives greater space to, and a more careful study of, matters pertaining to the endocrine sexual pathology of woman.

menopause. [Among the more recent German writers Aschner¹⁸ presents a brief consideration of the climacteric as affecting, and as affected by, the endocrine glands, without, however, treating it as an entity, a syndrome, based upon a reorganization, in general, of the hormonopoeitic system.—C. C.] Of the American writers Sajous¹⁹ is equally brief, merely referring to the menopause in his chapter on syndromes originated by disturbances of the internal secretions of the genital organs. In Barker, Hoskins and Mosenthal's monumental encyclopedia devoted to endocrinology and metabolism²⁰ the parsimony with which this subject is treated stands in sharp contrast to the great space given to all other endocrine problems.

Concerning the "pluriglandular theory" of the menopause—that is, regarding it as a complex "endocrine crisis" not as a simple hypoovarian phenomenon—early references are even less frequent. Bailleau²¹ conjectured that the thyroid might be the cause of the tachycardias which are so common in this period of life. In considering a case of Basedow's disease, originating in the menopause, Burr²² wonders whether the same thyroid upset which began the disease might not be the cause of some of the symptoms presented by women in the climacteric, particularly those symptoms more or less closely resembling hyperthyroidism. Vermorel²³ boldly asserts that this thyroid disturbance occurs in the climacteric, and in the same year Gluzinsky,²⁴ speaks of the possible intervention of the thyroid and of the suprarenal glands in the development of the symptomatology. A similar rôle is assigned by Pende²⁵ to the thyroid, and finally Schuster²⁶ attributes to the intervention of the suprarenal glands

¹⁸Aschner, B: *Beziehungen der Drüsen mit innerer Sekretion zum weiblichen Genitales, von Biologie u. Pathologie des Weibes* (Halban-Seitz), 1924, I B.s. 692. Urban und Schwarzenberg.

¹⁹Sajous: *The Internal Secretions and the Principles of Medicine*, ed. 10, Philadelphia, 1922. F. A. Davis Co.

²⁰Barker, Hoskins, and Mosenthal: *Endocrinology and Metabolism*, New York, London, 1922 (5 vols.)

²¹Bailleau: *Des tachycardies de la ménopause*, Paris, 1905.

²²Burr: *The Thyroid Gland and the Menopause*, Boston Med. and Surg. Jour., 1899, cxli.

²³Vermorel: *De l'origine thyroïdienne de certaines tachycardies ou palpitations dites nerveuses de la puberté et de la ménopause*, *Zentralbl. f. Gynäk.*, 1909.

²⁴Gluzinsky: *Einfige Bemerkungen zum klinischen Bilde des Klimakteriums*, *Wien. klin. Wchnschr.*, 1909.

²⁵Pende: *Op. cit.*, note 17, page 19.

²⁶Schuster: *Die Klimakterische und präklimakterische Atherosklerose, eine Folge innersekretarischer Störungen*, *Fortschritte der Medizin*, 1910. I published a translation of this interesting work with critical commentary in the *Revista Clinica de Madrid*, 1910.

certain of the characteristic climacteric symptoms, such as vasomotor disturbances and arterial hypertension. The studies of various other writers, pertaining to this same point, will be considered in subsequent chapters.

But the theme had not been discussed in its entirety, that is, regarding the menopause as a crisis involving the endocrine system as a whole, prior to my lectures in the Athenaeum at Madrid in January, 1915.²⁷ At that time I established all the essential points of this theory which was later developed by Culbertson²⁸ in almost the same way. Although averse to bringing up questions of priority, I would emphasize this chronologic fact.

Since the first edition of this book, the literature on the critical age in its relation to the internal secretions has increased, and it would be impossible to summarize it here. I shall mention only Carrillo's thesis²⁹ and the volumes by Blair Bell,³⁰ Bandler,³¹ Berman,³² Zondek,³³ Bayer and Velden,³⁴ Bauer,³⁵ and Hirsch.³⁶ Even in studies chiefly literary in character, such as that of Gallichan,³⁷ allusion is frequently made to the endocrine pathogenesis of the climacteric. Perhaps the exuberance aroused by this theme has been excessive, as has been the case in general with everything relating to the internal secretions. Indeed, this use of biologic ideas by pseudoscientific or manifestly unscientific persons has contributed not a little to the criticism which endocrinology encountered in past years and which has cropped up again recently.

Factors in the Menopausal Crisis

Of what does the "endocrine crisis of the menopause" consist? Or, in other words, what glandular elements usually take part in

²⁷Marañón: Op. cit., note 1, page 18.

²⁸Culbertson: A study of the Menopause with Special Reference to Its Vasomotor Disturbances, Surg. Gynec. and Obst., December, 1916. Undoubtedly this is the most suggestive study on the menopause appearing in recent years, although various views which the author holds do not agree with mine.

²⁹Carrillo: La Menopausia, Buenos Aires, 1919.

³⁰Blair Bell: The Sex Complex, London, 1916.

³¹Bandler: The Endocrines, Philadelphia and London, 1920.

³²Berman: The Glands Regulating Personality, The Macmillan Co., New York, 1922.

³³Zondek: Die Krankheiten der Endokrinen Drüsen, Berlin, 1923. J. Springer.

³⁴Bayer und von den Velden: Klinisches Lehrbuch der Inkrebologie und Inkretotherapie, Leipzig, 1927.

³⁵Bauer: Innere Sekretion, Wien, 1927.

³⁶Hirsch: Handbuch der inneren Sekretion, Leipzig, 1927 (On the press).

³⁷Gallichan: The Critical Age of Woman, London, (no date).

it? I believe *these three, the genital, the thyroid and the supra-renal are the fundamental glandular elements* entering into the development of this crisis. These three intervene more or less constantly in the somatic and functional transformation which characterizes the change of life. In my opinion the *hypophysis* has a more secondary rôle, although probably it frequently takes part in the crisis. I shall consider these three factors separately and in my analysis consider both the clinical features and all the climacteric phenomena in due order. At the same time I shall present a new pathogenic interpretation of the climacteric.

CHAPTER II

THE OVARIAN FACTOR

Ovarian Atrophy

The fundamental element of the menopause, but by no means the only one, is insufficiency of the ovary. This insufficiency corresponds to a process of atrophic sclerosis of the gland which has been well studied histologically by different writers and particularly by Kisch.¹ Macroscopically the ovaries shrink in size and harden until, as time goes on, they acquire a horny consistency. On microscopic examination, a considerable increase of connective tissue is observed which proliferates from the periphery to the center and causes the remaining ovarian elements to atrophy. Vascular sclerosis is also very manifest. In the graafian follicles typical changes occur which Kisch reduces to three phases. In the first phase the membrane of the follicle and its cavity remain unaltered, but the cavity is filled with fatty droplets, indicative of a frankly retrogressive process. In the second phase, or that of vesicular degeneration, the membrane of the follicle is wrinkled and folded, its cavity is reduced in size and is filled with a watery substance, containing cells, vascular remnants and such débris. In the third phase the follicle has been converted into a lengthened fibrous mass, in which a space, a trace of the former cavity, may yet be perceived.

The interstitial tissue atrophies and disappears, being replaced by adult fibrous tissue. This applies chiefly to the medullary portion of the ovary, since in the cortex the interstitial cells disappear much more slowly (Goodall²).

Naturally along with this anatomic regression there occurs a correspondingly progressive attenuation of ovarian activity. This fact used to be recognized only through the disappearance

¹Kisch: Op. cit., note (13), page 19.

²Goodall: The Morphological Pathology of the Ovaries as Endocrine Organs, in Endocrinology and Metabolism, Barker, etc., ii.

of so ostensible a manifestation as menstruation. But it is evident that mere amenorrhea is not the whole story. We now realize that the problem is much more complex than was believed only a few years ago, for besides its influence on menstruation, the ovary takes part in various other activities of the organism, as we shall soon see.



Fig. 1.—Section of a senile ovary (Novak).

Is Ovarian Insufficiency the Primary Factor?

Before entering upon the analysis of ovarian insufficiency, it is interesting to inquire whether the decline of ovarian function occurs spontaneously or is induced by other preceding glandular changes. Although without definite proof, it is this last supposition which I accept as the basis for an hypothesis which may be stated as follows: The continuous change which occurs during the course of life in the activity of the different ductless glands so prepares the ground that, at a certain time, functional decline

of the ovary begins. The moment for this decline may arrive spontaneously, or it may come prematurely through the appearance of other exogenous factors such as emotions or various diseases.

Indeed, clinical evidence of thyroid, suprarenal and hypophyseal changes, which I shall describe presently as more or less characteristic of the climacteric period, appear before the ovarian insufficiency, properly speaking, begins to be manifest. And such evidence, as well as experimental research, teaches that it is precisely these changes which predispose to the ovarian decline. It may be assumed, then, that by midlife something occurs analogous to that which happens in puberty. At this earlier period the genital explosion is preceded by a series of morphologic, psychic and other phenomena due to a "preparatory" influence on the part of the other ductless glands. The particularly significant change lies in the retrogression of the thymus or perhaps of the pineal gland, which announces the sudden, or explosive activation of the gonad. Turning to the changes at the menopause, perhaps a physiologic decline in hypophyseal efficiency may mark the beginning of general decadence.

Complexity of the Internal Secretion of the Ovary

Whether or not this hypothesis be accepted and whether or not ovarian insufficiency is primary or secondary, the fact remains that such insufficiency does occur eventually. Hence its consideration is of first importance. But, as has been indicated, the problem has become a more complex one than was once thought. The earlier belief, that there was a single ovarian hormone and that this dwindled away more or less rapidly as the atrophic process in the ovaries advanced, is no longer tenable.

On the contrary, according to the present point of view the internal secretion of the ovary is very complex. Yet this statement which is based upon clinical and experimental observation does not agree with chemical and anatomicopathologic evidence. When a woman's ovaries are extirpated or disease spontaneously destroys them, there is produced, varying with the age and general condition of the patient, not only functional annulment of the gland, that is, cessation of menstruation and concep-

tional incapacity, but also a whole series of anatomic and physiologic modifications in various organs and systems, some of which appear to be outside the realm of genital collaboration. No clinician, therefore, can subscribe to the conclusion drawn by Moulonguet-Doleris,³ that "the ovarian gland does not seem to have a very definite action on the general economy, notwithstanding all that has been said to this effect." Certain general manifestations do arise coincidentally and these may be divided into three groups, *genital*, *sexual*, and *general*.

The genital manifestations of the first group arise from the cessation of the primitive genital function and are, therefore, the suppression (a) of ovulation, (b) of menstruation, and (c) of the power of conception. The second group, the *sexual*, includes changes in morphology and in sex psychology. Primary and secondary sex characteristics, in the classic sense, are profoundly modified in case of ovarian destruction, a change seen with exceptional clearness in the young. Atrophy of the genital organs, irregular growth of the skeleton, heterosexual tendency in body development, irregularities in the growth of hair both general and sexual, the persistence of an infantile psychology, and eunuchoidism or masculinism are the changes here implied. Finally, in the *general* group appear those alterations occurring in organs and systems remote from the sexual. These are characterized by metabolic disturbances, with their usual tendency to obesity, by vasomotor symptoms, and by certain disturbances of the central nervous system.

I described these three groups in another publication⁴ and the contribution has been accepted by various contemporary writers, among them Leopold-Levi⁵ and Torre Blanco.⁶ The appearance of these changes brings up a most important question, whether they represent reactions corresponding to different internal secretions or are various expressions of reaction to a single cause, modified by certain factors such as conditions due to age, temperament, varying pathologic entities, or the intervention of en-

³Moulonguet-Doleris: La glande à sécretion interne de l'ovaire humain. Paris, 1923.

⁴Marañón: Clínica de la insuficiencia ovarica, Rev. Esp. de Gín. y Obst., April, 1917.

⁵Leopold-Levi: Opotherapie endocrinienne, Paris, 1922.

⁶Torre Blanco: Concepto actual de la glandula de la pubertad femenina, Arch. de Medicina, Cirug. y Especialidades, No. 8, 1921.

doocrine hormones, distinct from the ovarian. The discussion of this point leads directly into one of the most abstruse subjects of endocrinology, that referring to the normal and pathologic physiology of the ovary and its structure from the endocrine point of view. Since there is, as yet, no detailed exposition of the problem, I shall set down certain facts here for the better understanding of the following chapters.

The first supposition mentioned, that the internal secretion of the ovary is composed of various hormones, each one of which exercises a different series of influences in the organism, is founded solely on inductive argument, since we have no precise data on ovarian chemistry. [The experimental work of Allen and Doisy⁷ with respect to this problem is most interesting and important. This shows that the ovarian hormone exists in the liquor folliculi, probably produced under the influence of maturing ova by their follicle cells. Its production is evidently common to all female animals and it is not species-specific. In pregnancy a similar substance is apparently produced by the placenta. Zondek and Robinson⁸ in 1924 and Zondek and Ascheim⁹ in 1926 have also succeeded in establishing with fair certainty the presence in the follicle and corpus luteum of a substance capable of producing typical reactions. Their work is also based upon laboratory experimentation. Ascheim¹⁰ found an ovarian hormone in the placenta, in the blood of the pregnant woman not earlier than the fourth month, in the corpus luteum of pregnancy at times, and in the ovarian cortex in pregnancy; also in blood taken from the umbilical cord. With Zondek he found that the hormones from the anterior lobe of the hypophysis induces the formation of large follicles and corpora lutea in the ovaries of very young mice. Similar results were produced with the corpus luteum of pregnancy, the placenta and the serum (after the fourth month) from pregnant women and by implantation of the decidua of pregnancy.*—C. C.] In experimental study of the action of the ovary's internal secretion either the whole liquid

⁷Allen, E., and Doisy, E. A.: An Ovarian Hormone. *Jour. Am. Med. Assn.*, 1923, lxxxii, 819.

Allen, E., Pratt, J. F., and Doisy, E. A. The Ovarian Follicular Hormone. *Jour. Am. Med. Assn.*, 1925, lxxxv, 399.

⁸Zondek, B., and Robinson, M. R., *Am. Jour. Obst. and Gynec.*, 1924, viii, 83.

⁹Zondek, B., and Ascheim, Wien. *Klin. Wchnschr.*, 1926, v, 400.

¹⁰Ascheim, S.: *Med. Klinik* 1926, xxii, 2023.

*Cf. comment on work of C. C. Norris, page 158.

obtained from the gland by expression or partial extracts of this juice are used. The latter are procured by chemical processes more or less perfect but empiric. But we do not know whether this liquid, partial or total, contains various hormone principles or whether each one of these principles controls one of the activities of the total extract. Entering into the field of speculation, it is not venturing too much, perhaps, to express my belief in the probability of multiple ovarian hormones. I cautiously proposed such an hypothesis some years ago,¹¹ and it has come to be accepted by almost all recent writers among whom may be cited as authoritative, Athias,¹² Lipschütz,¹³ Stolper¹⁴ and Pende.¹⁵ In the case of one well-known product of external secretion, the pancreatic, for example, various substances enter into its composition which are endowed with diverse physiologic properties. In theory, therefore, it is not too much to state that an internal secretion may be composed of various principles, each one of which has a distinct endocrine function.¹⁶

Are the Different Ovarian Hormones Elaborated in Separate Portions of the Gland?

The structural complexity of the ovary appears to lend concrete support to the hypothesis suggested in this subtitle, inviting one to assign to each tissue in the organ the elaboration of one of the supposed hormones. As is known, the corpus luteum, the interstitial tissue, and the follicular epithelium represent three distinctly different types of cell structure, and these are re-

¹¹Marañón: *Op. cit.*, note (4), page 26.

¹²Athias: *Sur la secretion interne de l'ovaire*. *Arch. intern. de Physiologie*, August, December, 1921, xviii.

¹³Lipschütz: *Die Pubertätsdrüse und ihre Wirkungen*, Bern, 1919.

¹⁴Stolper: *Menstruation und das vegetative Nerven System*, *Wien. med. Wchnschr.*, 1923, lxxiii, Ref. in *Press. Med.*, 1923, No. 80.

¹⁵Pende: *Op. cit.*, note (17) page 19.

¹⁶Gley is one of the physiologists who with greater severity has criticized extreme endocrine hypotheses. He recently dwelt upon this concept of the plurality of the hormones in each secretion. (*Les Grands Problemes de L'Endocrinologie*, Paris, 1926.) He also concedes that each of the several principles of which a secretion is composed may behave differently in a pathologic state, which would explain the diversity of the clinical forms consequent to a lesion of a given gland, as the genital or the thyroid. Gley offers this explanation for so-called dysfunction. This same hypothesis has been advanced almost at the same time by another careful writer, DeQuervain. (*Zur Frage von der Disfunktion der innersekretorischen Drüsen*, Schweiz. med. Wchnschr., N. 35 1927.) In this connection it should be recalled that such was exactly the explanation of dysfunction which I proposed in 1916, in the second edition of my book *Las Enfermedades de la Nutricion y Las Glandulas de Secrecion Interna*. Madrid, 1916, doubtless unread by Gley although he cites my book in some of his.

garded, with greater or less unanimity, by various writers, as the endocrine tissues of the female genital gland.

In an effort to reduce the present discordant maze¹⁷ of literature to an outline containing only known facts or useful hypotheses, we may say: that the *internal secretion of the corpus luteum takes part, probably in a very complex way, in the menstrual process*, since the latter requires for its development the

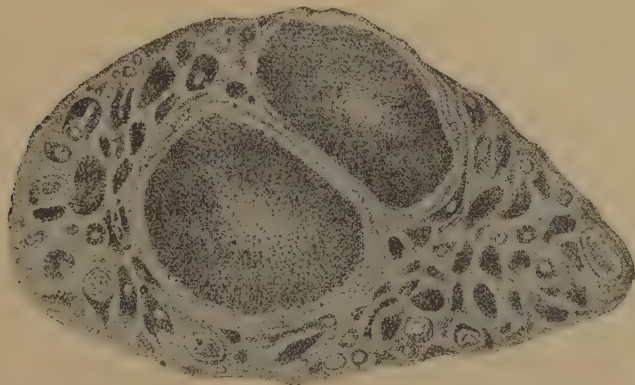


Fig. 2.—Section of an ovary from a virgin guinea pig, in heat. (Aschner.) Two very large corpora lutea are seen.

presence of lutein cell formation. Perhaps the opinion of Seitz and his collaborators¹⁸ is not far from the truth. They believe

¹⁷This statement is not exaggerated. I recommend to my readers the most authoritative and recent summaries on the endocrine function of the ovary: those of Swale Vincent (a), Evans (b) and Novak (c) in the *Encyclopedia Americana*; the corresponding chapters by Biedl (d) and Pende (e); Quinterno's thesis (f), Nubiola's monographs (g), Lipschütz' book (h), and I doubt whether there is anyone sufficiently clear-headed to find his way through the labyrinth of statements, negations and doubts which have accumulated on each one of these points in dispute.

(a) Swale Vincent: *Physiology of the Female Gonads*, Endocrinology and Metabolism, Barker, H. and M., ii, 1922.

(b) Evans: *The Rhythm of Gonadal Function with Special Reference, etc.*, in *Endocrinology and Metabolism*, B.H. and M., ii, 1922.

(c) Novak: *Influence of the Ovary on the Development of the Female Generative tract*, Endocrinology and Metabolism, B.H. and M., ii, 1922.

(d) Biedl: *Op. cit.*, note (15) page 19.

(e) Pende: *Op. cit.*, note (17) page 19.

(f) Quinterno: *La función de los cuerpos amarillos*, Buenos Aires, 1921.

(g) Nubiola: *Résumé of his work in El ciclo sexual de la mujer*, Policlínica Sevillana, 1917.

(h) Lipschütz: *Op. cit.*, note (13) page 28.

¹⁸Seitz, Wintz, und Fingerhut: *Ueber die biologische Funktion des Corpus Luteum: seine chemischen Bestandteile, usw.*, München. med. Wchnschr., No. 30, 1914. This includes a résumé of numerous previous publications of the Seitz group.

that the influence of the corpus luteum varies according to the time of its evolution. In its initial phase immediately following the rupture of the follicle, the young gland causes the cyclic transformation of the uterine mucosa, including the establishment of the menstrual flow. But the mature, fully formed corpus luteum elaborates a substance of contrary action, causing involution of the mucosa and cessation of the menses. According to these writers a different substance may be extracted from the corpus luteum in each of these two phases, protein in the early development (lipamine), lipoid in the mature state (luteolipoid). These exercise excitant and inhibitory action, respec-

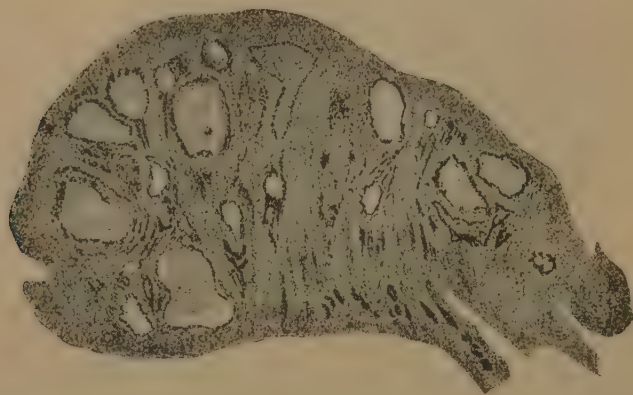


Fig. 3.—Section of an ovary from an infant aged three months. Here the interstitial tissue (shaded) is seen to be very developed. (Aschner.)

tively, on the menses, and correspond therefore to the two assumed categories of hormones coming from the corpus luteum. My experience in the clinical application of these extracts certainly leads me to a contrary view with respect to their alternately excitant and inhibitory efficacy. Nevertheless, the hypothesis is adjustable and can be made to correspond sufficiently well with clinical data so that, for the moment, it serves as a point for orientation in the reigning obscurity pertaining to this subject.

In the phenomenon of conception the influence of the corpus luteum is incontrovertible. The hormone undoubtedly *sensitizes* the uterine mucosa, making it suitable for nidation of the ovule

and the formation of the placenta. Further than that, it inhibits ovulation during the entire period of gestation. It is not too much to say, therefore, that *the hormones which I term genital, those which regulate the menstrual and conceptional phenomena, depend upon the corpus luteum.* [The outstanding work in the recognition of a specific hormone is that of R. T. Frank and his associates,¹⁹ who have been working on this problem for many years. Their results are based on experimental study of ovarian physiology in the lower animals, but seem to have come to a place where these results are about to reach clinical application in woman. These investigators have succeeded in recovering from the follicular liquid, the corpus luteum, the placenta and blood of females in estrus a substance which they call the "female sex hormone." Inasmuch as the corpus luteum succeeds the follicle and the placenta the corpus luteum, the term "gestation gland" is offered as a suitable appellation for this triad. This active substance is a thermostabile liquid of high molecular weight and must be so prepared as not to give cholesterol reaction.—C. C.]

The interstitial tissue, or so-called diastematic gland, probably elaborates the sexual hormones. These preside over feminization, by which I mean the development of the primary and secondary sex characteristics. This idea has been emphasized by the transplantation experiments of Steinach,²⁰ Voronoff,²¹ Pezard,²² Athias,²³ Lipschütz,²⁴ and many others, until it becomes difficult to doubt further. Swale Vincent,²⁵ formerly severe in his criticism, now recognizes that the majority of writers are in

¹⁹Frank, R. T., Frank, M. L., Gustavson, P. C., and Weyerts, W. W.: Jour. Am. Med. Assn., 1925, lxxxv, 510. This preliminary report was followed by a number of short articles at frequent intervals in the same Journal.

Frank, R. T., et al.: The Occurrence and Present Chemical Status of the Female Sex Hormone, Endocrinology, 1926, x, 260.

Frank, R. T.: Function of the Ovary, A Résumé—Fifth Paper. Am. Jour. Obst. and Gynec., 1926, xli, 585.

²⁰Steinach: Verjüngung, Berlin, 1920.

²¹Voronoff: Vivre, Paris, 1920.

²²Pezard: Développement expérimental des ergots et croissance de la crête chez les femelles des gallinacées, C. R. de l'Acad. des Sciences, February, 1914, and February 1915.

Idem: Le conditionnement physiologique des caractères sexuels secondaires chez les Oiseaux, Thèse de Paris, 1918.

²³Résumé of the excellent work by Portuguese physiologists in op. cit., note (12) page 28, and Etudes histologiques sur la griffe ovarienne. Libro en honor de D.S. Ramon y Cajal, Madrid, 1922, Tomo 11.

²⁴Lipschütz: Op. cit., note (13), page 28.

²⁵Swale Vincent, note (17a), page 29.

accord on this subject and is inclined to the same opinion. The corpus luteum can play no rôle in this situation since feminization of the individual is evident before puberty when there are no such bodies. The probability that this hormone is produced by the interstitial tissue, although it may originate in the follicular epithelium, is shown by transplantation of the ovary in the castrated male. When such a graft, free from corpora lutea, is successful, feminization of the castrated male becomes readily apparent. [The fact that a grafted portion of ovarian tissue may "take" does not prove that it functions in so far as to produce a hormone. This is particularly apt to be the case with transplanted interstitial portions of the gland. Or the engrafted portions living may be so small as to give an inappreciable reaction even if they are active.—C. C.]

A primary endocrine value is attributed by some to the follicle. A writer as authoritative as Athias states that "the hypothesis of the endocrine rôle of the follicular elements has gained ground in recent years." But along with the work already cited of Steinach, Lipschütz, and others, MacIlroy's investigations²⁶ have demonstrated that the interstitial cells persist in grafted ovarian tissue much longer than do the follicles and that uterine atrophy and regression of sex characteristics are not seen while these interstitial cells persist. A more forceful objection to the theory that the interstitial cells produce a hormone lies in their inconstancy in the animal species, thus making it impossible to assign to such tissue any function not transient. But this objection has been met by Athias²⁷ with the demonstration that this lack of constancy is more apparent than real, minute histologic studies having shown more or less extensive portions of interstitial tissue capable of activation in animal species in which such tissue was believed not to exist.

[Here again we see the possibility that results obtained by experimental investigation may not hold good for the human species. While the conclusions of this writer may hold good in woman, clinical gynecologic experience has been unable, thus far, to prove it.—C. C.]

²⁶MacIlroy, L.: Some Experimental Work upon the Physiological Function of the Ovary, *Jour. Obst. and Gynec., Brit. Emp.*, London, 1912, xxii.

²⁷Athias: *Op. cit.*, note (23), page 31.

According to experimental data which we now possess, there is relatively little chance of assigning to any special part of the gland that function of the ovary which I have designated as *general*. At least no such localization is possible as has been assigned to the genital and sexual functions. It is entirely probable, indeed, that the more general upsets such as circulatory disturbances, nervous manifestations and metabolic irregularities observed after cessation of ovarian function, are really systemic. They may be due, not so much to the loss of certain ovarian hormones, as to reaction on the part of other ductless glands and of the nervous system, all of which were previously normal.

In any event, certain writers, among them Athias,²⁸ are not inclined to admit this "division of labor" on the part of the different ovarian elements. They regard it as "more likely that the secretion is the product of the conjoint metabolism on the part of the various structures which permanently or temporarily make up the ovarian economy." On the other hand, the majority of writers agree on the multiplicity of these hormones.

Attempts to Isolate the Different Hormones Chemically

The efforts of Seitz, just mentioned, to isolate two substances, lipamine and luteolipoid, differing in action, appear to place a chemical foundation beneath the hypothesis of the hormone. This hypothesis, if verified, might explain the multiplicity of these secretions. Iscovesco²⁹ made a like attempt. He separated different lipoids of different physiologic activity from the total ovarian extract.

Furthermore, Itagaki³⁰ has obtained from the gland two principles, one soluble in alcohol and capable of activating uterine movements, the other soluble in water but insoluble in alcohol and inhibiting these movements. The work of Quintero³¹ and others has produced similar results. It is possible, as Chauffard and his associates think, that cholesterin, so abundant in the ovary, is one of the hormonie principles. Nevertheless, it must

²⁸Athias: Op. cit., note (23), page 31.

²⁹Iscovesco: Les Lipoides de l'ovaire, du corps jaune et du testicule, Presse, med. 1912. (Résumé of his work).

³⁰Itagaki: The Influence of Corpus Luteum Extracts upon Plain Muscle, Especially that of the Uterus, Quart. Jour. Exper. Physiol., 1917, xi.

³¹Quintero: Op. cit., note (17f), page 29.

not be forgotten that all attempts to isolate such hormones as chemical substances have failed. [See reference to Frank's work, previously cited.—*C. C.*]

By way of summary, we may say that in considering the climacteric the theory of multiple ovarian hormones is of value in interpreting many of the phenomena appearing during this period of life. It is for this reason that I have dwelt upon this question. Keeping in mind all these reservations and all the probabilities, we may still say that the ovary expresses its function in three ways, or by three means—genital, sexual and general—which perhaps correspond to three separate hormones elaborated in different parts of the gland.

During the individual's period of growth, if some pathologic process intervenes and destroys the ovaries, the whole organism at once shows the lack of these three hormonal activities. If the ovaries are extirpated this effect is seen even more clearly. The genital function immediately disappears—menstruation ceases, conception is impossible. If the subject is a girl of pre-pubescent age the lack of the sex hormone is evident in that the genital tract does not take on its mature development at puberty and the secondary sex characteristics, which from the morphologic point of view distinguish her from man, fail to appear. On the other hand, if the woman has reached maturity, the essential feminine characteristics tend to become obliterated. Finally, the absence of the general hormone is manifested in the childish or exaggerated mentality of the castrate, in intense vasomotor reactions, in the tendency to obesity and like symptoms, all of which are more marked in proportion to the age of the patient, as I shall explain later in detail.

Clinical Dissociation of the Menopause and Climacteric

If, instead of this sudden, total suppression of ovarian function, there is a gradual, physiologic loss, such as takes place at the climacteric, the resulting disturbance is manifested in a very different way. Then the change, far from being abrupt, is so gradual that insufficiency on the part of certain groups of hormones may be compensated for by other groups.

From the first I have endeavored to avoid the common error of combining in a single concept the disturbances characterizing the climacteric with those of the menopause which connotes simple suppression of the menstrual flow. The irregularities of menstruation, its gradual decline and finally its cessation indicate that one group of hormones only, the genital, elaborated probably in the corpus luteum, has become deficient. Other ovarian secretions, however, the sexual and the general, elaborated by the follicular and interstitial tissue, may continue, or, on the contrary, may have been exhausted for some time. The result is that in the greater proportion of women we see a clinical expression of instability some time prior to the real menstrual irregularities. Various indications of changes in sexual function or in sex morphology appear, particularly the different nervous and vasomotor symptoms as well as those of metabolic disturbances. This fact is particularly important since the psychic disturbances, to be described later, frequently precede other irregularities by a considerable period of time. The same thing is revealed in the unequal deposit of adipose tissue, the so-called menopausal obesity, a common change coincident with the climacteric and accepted as one of its most characteristic features. But when this coincidence is studied accurately, the clinician is surprised to note that his statistical observations show that obesity does not coincide with the menopause, but is usually in process of development some time prior to it. This is evident in Kisch's³² tabulations; and von Noorden³³ reached similar conclusions. Kisch and von Noorden, however, fix the onset of the climacteric arbitrarily in the year of the menopause without considering as climacteric the preceding phenomena; hence their statistics are worthless from my point of view. I believe that this obesity is a climacteric symptom, as clinical observation teaches us, and as legitimately a part of ovarian insufficiency as amenorrhea itself.

The contrary condition is also observed, although less frequently does menstrual cessation precede the development of obesity, the nervous disturbances, and the other symptoms dependent upon insufficiency of the general hormones. It will be

³²Kisch: *Op. cit.*, note (13), page 19.

³³Von Noorden: *Die Fettsucht*, Wien, 1910.

shown later that in cases of ovarian extirpation or of sudden premature menopause this type of dissociation is very frequent.

Stages of the Critical Age

If the foregoing be accepted by way of explanation, it then becomes possible to consider the critical age as divided into three periods or stages which may be called (1) *premenopausal*, (2) *menopausal*, and (3) *postmenopausal*. The first stage extends from the appearance of the first general symptoms to the beginning of menstrual irregularities. The second embraces that period during which menstrual irregularities obtain, and the third comprises the time after the cessation of all menstruation until the disappearance of the general climacteric symptoms.

Preclimacteric Ovarian Hyperactivity and Ovarian Instability

Before leaving this discussion of ovarian function, mention should be made of the opinion held by certain writers that the decline of ovarian activity is likely to be preceded by a period of hyperactivity which represents, as it were, a final supreme effort. According to Pende,³⁴ among others, this first phase of sexual hyperfunction is characterized by more frequent and increased menstruation, the "functional uterine hemorrhages" described by American writers. Other characteristics are proliferative changes in the mucosa and even in the uterine muscle itself, congestion and hyperesthesia of the external genitals, together with an increase in the sexual reaction even to the extreme of erotomania and nymphomania. [The *metrorrhagia myopathica*³⁵ of American writers, also known as "essential uterine hemorrhage," is regarded as due to changes taking place in the uterine wall itself rather than to ovarian dysfunction. This condition has been ably described in the English literature, chiefly by Fletcher Shaw.³⁶—C. C.]

In my opinion there is no reason to accept this idea of ovarian hyperactivity. The symptoms enumerated by Pende are not suffi-

³⁴Pende: Op. cit., note (17), page 19.

³⁵Anspach: *Metrorrhagia Myopathica*, Am. Jour. Obst., January, 1906, also Surg., Gynec., and Obst., 1909, ix, 315.

³⁶Shaw, W. Fletcher: *Chronic Metritis and Allied Conditions*. New Syst. of Gynecology, (Eden-Lockyea) 1917, Macmillan. Also Jour. Obst. and Gynec. of the British Empire, 1914, xxvi, 73.

cient to indicate an excessive genital function. Frequent and repeated hemorrhages, to which further consideration will be given presently, find their explanation within the hypothesis of ovarian insufficiency. The congestions of the external genitalia are passive phenomena also observed in other organs and portions of the body. As for the states of exaggerated sexual instinct shown by women—and by men—passing through the climacteric, they are certainly the effects of psychic mechanism due to humeral stimuli not alone ovarian but also thyroid in all probability. These reactions may be abnormal but they are not purely the consequences of increased gonadal secretion and do not always coincide with the first stage of the change. Furthermore, such sexual exaggerations are frequently prolonged until after the disappearance of all evidence of ovarian activity, and there are even cases in which they begin late, in the postmenopausal stage, the prolongation being due to a purely psychic mechanism, a mere remembrance of sexual feeling, now definitely extinguished.

While refusing to admit this theory based upon genital hyperactivity, neither do I desire to claim that the decline of ovarian secretion is accomplished by a smoothly descending curve. On the contrary, the curve of this decline is undulating, with ups and downs varying in length in every case. Some more fortunate individuals pass through the climacteric transition in three or four months during which the diminution of genital function is steadily progressive with only a mild general reaction. Others suffer for years the local and general effects due to the loss of an organ which violently resists its extermination. Between these two extremes are patients who express the reaction in every variety of degree.

These sudden and irregular fluctuations in the production of the internal secretion of the ovary are especially marked at the beginning of the climacteric, constituting the phase which we may call ovarian instability and which helps to explain variation in clinical manifestation during this period of life. This concept of *instability* will appear again and again as we take up each one of the glandular elements which collaborate in the menopausal crisis. *Pathogenically and clinically the critical age is characterized by instability.*

CHAPTER III

THE THYROID FACTOR

Thyroovarian Synergy

Ovarian insufficiency is the central factor of a complex neuro-endocrine crisis of as great interest as the ovarian change itself. In this *climacteric crisis* the thyroid and suprarenals intervene constantly and perhaps the hypophysis does also.

The thyroid enters the situation in nearly every climacteric case. Its function varies in intensity, according as the reaction produced by the crisis approaches or recedes from the normal state. This conclusion has been developed out of physiologic and clinical study.

So intimate, indeed, is the fundamental correlation between the thyroid and the genital gland that the disappearance of the latter constantly causes a thyroid reaction. This reaction is observed as much following experimental or clinical extirpation of the ovary as in the spontaneous functional conflicts through which the ovary passes in the course of life—puberty, menstruation, pregnancy, and lastly the menopause. In all of these cases the thyroid reacts in one of two ways; either underfunction, *hypothyroidism*, or overfunction, *hyperthyroidism*. At times, of course, this reaction does not develop clearly. Then the clinical appearance is that of a mingling of, or at least a very rapid succession of, the manifestations corresponding to hyperthyroidism with others that are hypothyroid. The resultant syndrome has as little physiologic consistency as it has evident clinical reality and is called *dysthyroidism*. This is Levi and Rothschild's *thyroid instability*¹ or Pende's *paradoxical partial hyperthyroidism*.²

At present we do not know the explanation of these variations.

¹Levy and Rothschild: *Etudes sur la physio-pathologie du corps thyroïde*, Second series, Paris, 1911.

²Pende: *Op. cit.*, (17), page 19.

In the presence of an apparently identical stimulus—ovarian insufficiency—one woman's thyroid will react with excessive function and that of another with decreased function. But it may be presumed with sufficient probability that such a difference *depends on the previous state of the endocrine system* which in some women, particularly in certain periods of life, is more inclined to the hyperfunctional reaction and in others to the hypofunctional. We may follow a comparison which has already served us, that things happen in the field of the internal secretions as in that of the external. Taking the gastric secretion, for example, we are used to seeing the same abnormal stimulus—a bromatologic disorder—produce symptoms of hyperchlorhydria in one stomach and hypochlorhydria in another. Or again, one type of reaction succeeds the other in the same individual in the course of a few days. In my belief these differences depend, without doubt, on a previous state of gastric function, such as a different reactional aptitude on the part of each gastric mucosa.

An unquestioned fact, already noted in a previous contribution,³ is that the hypothyroid reaction is much more frequent in the ovarian insufficiency of young women, as in cases of retarded puberty which is so often accompanied by more or less pronounced hypothyroidism. On the contrary a hyperthyroid reaction is observed much oftener in the ovarian insufficiency of adult women, particularly at the normal climacteric age.

The intervention of the other glands, particularly the suprarenals, complicates the situation. The incidents of the genital life, which are so complex in many women, have their importance. Multiple exogenous factors such as emotions, infections, and intoxications are influential. During the course of life these leave an impression upon the endocrine and the nervous systems. All these factors, and others which still elude us, predispose the thyroid to hyperfunction. The result is that *climacteric hyperthyroidism*, more or less masked, appears in an extraordinarily large number of women—at least in southern Europe.

An analysis of the arguments upon which this statement is founded may be formulated as follows:

³Marañón: Op. cit., note (4), page 26.

The State of the Thyroid in Castration. Influence of Age

In the first place, in the experimental field it is not unusual to observe that castration is followed by thyroid hypertrophy. Parhon and Goldstein^{4, 5} have noted that in castrated animals the thyroid gland increases in size, this increase being due apparently to pronounced congestion and a significant distention of the follicles by colloid substance. Other writers have confirmed these findings. But, in general, the experimental argument has little value here, as cannot be stated too often, since there is no comparison between the simple reactions occurring in the organism of a rabbit or cat suddenly deprived of its ovaries, and the extremely complex and diverse reactions which the gradual extinction of her sexual function produces in a mature woman, subject to a thousand modifying influences. On the contrary, if the castrated animal is a young male, not only does this thyroid hypertrophy not take place, but a total atrophy of the gland occurs with change to characteristic fetal structure (Biedl⁶) (Pende⁷). I have not found hypertrophy of the thyroid in many rabbits castrated soon after birth and examined some time later. In the face of such apparent contradiction in experimental findings the force of any demonstration is destroyed. But the contradictory findings are logical, for experiments cannot provide schematic demonstrations of a hypothetic proposition. It is too often forgotten that an organism, although it be as simple with relation to the human being as that of a frog, is not a test tube wherein chemical elements of known reactive power may be placed. The experiments are abandoned long before the supreme biologic moment. My opinion is that such experiments are of little value. The changes observed in a castrated rabbit can give us but a vague idea as to what goes on in the organism of a menopausal woman and we should not value them too highly. The size of the thyroid is really independent of its functional capacity, as is seen by the innumerable cases of hypothyroidism with thyroid hypertrophy and of hyperthyroidism with small thyroids. Therefore, instead of striving to determine the size of the thyroid we should seek to

⁴Parhon and Goldstein; *Les sécrétions internes*, Paris, 1908.

⁵Parhon and Goldstein; *Traité d'Endocrinologie*, Jassy, 1923.

⁶Biedl: *Op. cit.*, note (15), page 19.

⁷Pende: *Op. cit.*, note (17), page 19.

determine the functional ability of the gland as expressed in other more significant reactions. In such cases we find that it is frankly hyperfunctional. For example, I have shown⁸ that in rabbits castrated some time previously the ingestion of thyroidin causes a more rapid emaciation and a greater excitability than in uncastrated rabbits. Moreover, in the former it is possible to obtain positive exophthalmos, while it is almost impossible to produce it in noncastrated animals, however much they may be intoxicated with enormous doses of thyroid.

This means that, *independently of the size of the gland, castration creates, if not an actual active hyperthyroidism, at least a hyperthyroid predisposition.*

Much more interesting, naturally, are the results obtained in the castrated human being. Yet in these the fact observed in animal castration is repeated, namely, that the sex, age, and like factors notably influence the form of thyroid reaction. Tandler and Gross, for example,⁹ in the cadaver of a young eunuch found sclerotic atrophy of the thyroid, the weight of which was only thirteen grams. Pende¹⁰ has noted that in oriental eunuchs and in the Russian "skoptsy," castrated before puberty, the thyroid does not increase in size, but, on the contrary, cannot be palpated or if palpable is shrunken and hard. In the last few years I have seen a number of male children with more or less marked genital insufficiency and in one only was thyroid hypertrophy observed, a finding in this case which I regarded as being usual for deep and careful palpation of the thyroid lobes showed them to be small and hard. On the other hand, *in the woman castrated during adult life, it is common to see more or less apparent thyroid hypertrophy.* (Pende, Marañón.) *Hyperthyroid symptoms* especially are more marked proportionately as the age of the woman more nearly approximates that of the spontaneous crisis. Later I shall emphasize this point (already made classic by early writers) that, from the endocrinologic point of view, the symptomatology of the artificial menopause is distinct from that presented by spontaneous menopause.

⁸Marañón: Producción experimental del exophthalmos. Congreso de Valladolid para el Progreso de las Ciencias, 1915.

⁹Tandler und Gross: Die biologischen Grundlagen der sekundären Geschlechtscharaktere, Berlin, 1913.

¹⁰Pende: See note (17), page 19.

Hyperthyroid Symptoms in the Usual Menopause

But the most valuable demonstrations of this hyperthyroidism we shall find—along with other points in menopausal pathogeny—in our study of the menopause itself. In the first place *this study shows us that several of the climacteric symptoms which were considered as directly dependent on the lack of the ovarian secretion may be—indeed often are—hyperthyroid symptoms* either alone or in collaboration with other glandular disturbances. This is true of the tachycardia, palpitations, and particularly the emotional states, loss of weight and other less common symptoms, whose endocrine pathogeny will be discussed in more detail in the clinical part of this monograph. Now when a woman who is passing through the sexual change enumerates her complaints and among other symptoms says that she is suddenly seized with palpitations, that her weight varies without apparent cause, that she is in a constant state of uneasiness, as if some evil threatened her, that her nervousness magnifies the little contrarinesses of life, and when we note her exalted manner and her brilliant gaze, and find her pulse is 90 or more, that perhaps the thyroid is slightly enlarged (or at least deep palpation discloses congestion)—in the presence of this symptomatic picture, what true physician, knowing the hyperthyroid syndrome, is not impressed by its identity with this menopausal symptomatology?

In Chapter I it was explained that various writers have conjectured that some of the climacteric symptoms—those just enumerated, principally—have a hyperthyroid origin. *The present state of thyroid physiopathology permits us, in my judgment, to replace conjecture with confident statement. In many cases there are typically hyperthyroid symptoms. Note, I say “in many cases”—not in all.*

This explanation refers to cases of mild menopause with only slight pathologic upsets. But in a great number of women with more turbulent crises, this hyperthyroid reaction becomes much more pronounced and consistent. The *hyperthyroid syndrome* is then clearly revealed, with characteristics so distinct and constant that one may speak of *climacteric hyperthyroidism*. In another chapter I shall describe this condition. Here I shall comment only on its general pathology.

Pathologic Hyperthyroidism

From my own observation I can state that the highest percentage of hyperthyroid women begin to be so in the menopausal crisis, and that in almost all those who had been so previously the hyperthyroidism is aggravated on reaching the crisis. It is surprising that so little or no attention is given by writers to this important relation of hyperthyroidism to the menopause—with the exception of Pende,¹¹ Rankin,¹² Pineles,¹³ and Luscan.¹⁴ Since I first saw hyperthyroid patients this relation was one of the things which most attracted my attention, and as my experience widened, so my conviction as to the relationship was strengthened, and I made an effort both in my lectures and in my publications to draw attention to its existence.¹⁵ For all these reasons and because I am in a position to say a great deal, I stress this point which has so much importance in the development of my theory as to the climacteric crisis.

In the last ten years I have collected the clinical histories of 696 women affected with hyperthyroidism of all degrees of intensity and representing various clinical types which I give as follows: 1. *Classic Basedow's disease*. 2. *Simple hyperthyroidism*, often accessional in its different clinical forms, (a) *cardiovascular*; (b) *consumptive*; (c) *diabetic*; (d) *nervous*; (e) *digestive*. 3. *Basedowified simple goiter*. 4. *Cardiac goiter*. *Forty-three per cent of these women either began to suffer this complaint in the critical age, or had had a simple goiter which became toxic in this period.*

Of these patients, 25.6 per cent were women of forty-five to fifty years of age, that is to say, at the very end of the critical epoch. The menses had been scanty and irregular and many of them were sterile. In short, there had been indications more or less pronounced of ovarian insufficiency.

In 6.1 per cent of the cases the women were between twenty-

¹¹Pende: See note (17), page 19.

¹²Rankin: *The Climacteric Life*, Brit. Med. Jour., 1919.

¹³Pineles: *Ueber Iodbasedow im Klimakterium*, Wien. med. Wchnschr., 1923, No. 73.

¹⁴Luscan: *Goître exophtalmique et ménopause*. Thèse de Montpellier, 1923.

¹⁵Marañón: *El hipertiroidismo climacterico*. Lérida, 1922.

five and thirty; in these for various reasons "complete premature menopause" had occurred, at the close of which the hyperthyroidism developed.

Seven and nine-tenths per cent were hyperthyroid women between thirty-five and forty-five. These still retained the menses which were either profuse or presented other disturbances indicative of the approaching menopause.

Only 16.4 per cent of these women had retained normal menstruation. But even from this group 7 per cent may be set apart. In these, while normal menstruation still continued, there had been somewhere in the clinical history a genital episode closely related to hyperthyroidism such as serious abortions which were the starting point of thyroid disease. In some there was marked lessening of thyroid symptoms during the menstrual period, in others organic exhaustion through an excessive number of pregnancies very close together or similar physical drains.

Therefore, it may be stated that in the immense majority of cases of female hyperthyroidism its beginning coincides with states of ovarian insufficiency, and of these cases, the greater number are the ovarian insufficiencies of the critical age.

That is to say the distinct hyperthyroid reaction—so frequent among climacteric women—becomes intensified in a large group of these, even beyond pathologic limits, giving rise to a true hyperthyroid syndrome. In reality, these "pathologic limits" of which we speak are arbitrary. We cannot say where a physiologic hyperthyroid reaction ends and where the pathologic syndrome begins. A gradation of cases, insensibly progressive, extends from those women whose hyperthyroidism may be considered as only a *temperament*, a little accentuated by the circumstances, up to others affected with true Basedow's disease.

Influence of Predisposition, Emotion, Infections, and Therapeutic Abuses in Climacteric Hyperthyroidism

Whether the hyperthyroid reaction of the menopause will remain within discreet limits or will take great pathologic flights, depends essentially on two circumstances—on the previous predisposition of the woman and on whether there coincide with the menopause other favoring circumstances, as the menopause itself

with its hyperthyroid explosion or emotional states, infections, immoderate treatment with iodine or with thyroid extract. I shall return to several of these points in the chapter devoted to the general etiology of the climacteric symptoms.

The rôle of *predisposition* is clearly deduced from the observation of that group of women who acquire hyperthyroidism in the critical age. This group is constituted principally of those who previously presented a *hyperthyroid temperament*. These thin women, frequently very prolific, nervous, vehement, active, with large and expressive dark eyes, very black hair, unstable pulse, free perspiration, little sensitive to cold and very sensitive to heat, are those who presently suffer great hyperthyroid imbalance, which is merely their same temperamental signs morbidly accentuated. In these women—among whom I believe the most interesting of their sex are found—it is easy to predict several years before, the course which their menopausal symptoms will follow. Such a prophecy can be made not only in these cases, but for the other types of climacteric pathology, as we shall see later.

This influence of predisposition is observed with even greater clarity in the *cases of women with goiter*. *Twenty-one per cent of my cases of climacteric hyperthyroidism concern patients* who have had a simple goiter for many years, with those mild symptoms of “temperamental, constitutional hyperthyroidism” before mentioned, or without any symptoms. On reaching the critical age, through its action alone or through the collaboration of other causes which disturb the thyroid function, these women become frankly hyperthyroid. *Therefore, women with goiter, simple though it may be, should be subjected to special prophylactic treatment when the change of life occurs*, especially as regards the employment of thyroid and iodine medication.

The collaboration of other factors which excite thyroid secretion with the menopause is seen at once in the emotions. In every age the emotions are a frequent point of departure for hyperfunctional states in the thyroid, and they are much more apt to have this effect in the critical age, for then the field has been prepared in every way for hyperthyroid reactions to appear or

be increased. This aspect of the menopause is so important that I devote a special chapter to it. This brief comment must suffice for the present.

The same may be said of certain *infections*, whether of the *focal* type (so well studied by American writers) or of the *general* type—as acute rheumatism, erysipelas or influenza—which when occurring in this age may cause hyperthyroid attacks in predisposed individuals. However, this occurs much less frequently in this period than in youth. *Influenzal infection* is especially important from this point of view. During my wide experience at the time of the epidemic of 1918-1920, I frequently verified the determining action of influenza upon hyperthyroidism, especially in predisposed persons.¹⁶

Finally, the greatest importance attaches to *the action of immoderate treatment with thyroid or with iodine*, both being medical excitants of the function of the thyroid. It is known that in every stage of life the excessive ingestion of thyroid preparations is capable of causing typical and very lasting basedowic syndromes, true cases of *therapeutic hyperthyroidism*, some of which I have described.¹⁷ Naturally, this occurs much more easily in subjects predisposed to hyperthyroidism, and therefore those in the menopause. This fact is frequently observed, since the tendency to take on weight, which is natural in the climacteric, greatly worries women who seek every means to combat it, frequently on their own initiative or advised by unscientific persons. Commercial thyroid products are rather commonly resorted to for this purpose and women often take excessive doses. Von Noorden¹⁸ has noted that these menopausal women who abuse this medication, and even those who are under careful medical care, are singularly predisposed to suffer various thyrotoxic symptoms, which are not produced in other ages. Yet I do not believe, as he does, that this age is for that reason alone “a contraindication” for the employment of thyroid treatment in cases in which other reasons indicate it. I wish rather to stress the fact that in these years thyroid administration should

¹⁶Marañón: Gripe e hipertiroidismo, Archivos Españoles de Endocrinología. y Nutrición, 1924, No. 1.

¹⁷Marañón: La sange en un caso de tiroidismo terapéutico, Revista clínica de Madrid, 1912.

¹⁸Von Noorden: See note (33), page 35.

be managed with particular prudence, being ever on one's guard against the first evidence of thyroid disease *and preceding the treatment with a careful examination of the thyroid reactions.* Cases exhibiting any mild or minor signs of hyperthyroidism should not be given thyroid. Within this last category fall almost all who have goiter.

The same may be said of *iodine*. The abuse of this remedy gives rise, particularly in women predisposed to hyperthyroidism and especially those with goiter, to the explosion of hyperthyroid symptoms which may reach the complete Basedow syndrome, the *Iodbasedow*, of the Germans. I have observed a considerable number of such cases, since in Spain it is a common practice to treat goiter patients with progressively increasing doses of tincture of iodine up to very dangerous limits. However, it appears that latterly the number of these accidents has lessened, and perhaps this fact is due to my constant admonitions and those of my collaborators, Bonilla¹⁹ and others. Iodine, however, is valuable in *neutral* or *hypothyroid* goiters. Its use here is sanctioned by an empiric lay practice and confirmed by the work of contemporaneous Swiss investigators.^{20, 21} But, on the other hand, *like thyroid extract, it is useless and dangerous in every case of goiter with hyperthyroid symptoms, however sketchy these may be.* From this point of view, *the menopause or its proximity should be considered, barring exceptions, as a hyperthyroid predisposition, that is to say, as a contraindication for iodine, even in the absence of positive hyperthyroid symptoms.* (Pineles.²²)

Course of Climacteric Hyperthyroidism

This frequent and interesting *menopausal hyperthyroidism* is *likely to be transitory*, as Pende points out²³ and as I have confirmed. Naturally, it is more transient in proportion as it is milder. There is, at times, the perfect type of physiologic hyper-

¹⁹Bonilla: Contribución al estudio del tratamiento de los estados hipertiroides. Siglo Médico. 1919, No. 66.

²⁰See a Critical Résumé of the Question in Bonilla: Profilaxia y tratamiento del bocio per el yodo, La Medicina Ibero, 1923, No. 307.

²¹Vidal and Jordana: La profilaxia del bocio endémico por el yodo. Arch. Esp. de End. y Nutrición, 1924.

²²See Pineles: Note (13), page 43.

²³Pende: See note (17), page 19.

thyroidism which Brooks has described²⁴ in relation to the emotional, sexual, and other crises of life. He overlooks, however, just this particular one, the climacteric, which is the most interesting and complicated. The cases in which typical Basedow's disease is set up last longer, but I believe that it is not so in younger individuals in whom the process assumes the type of *malignant senile hyperthyroidism*. This form of the disease, of bad prognosis through its duration and through its consequences, really does not correspond to menopausal pathology.

When the hyperthyroid reaction disappears, the function of the gland may remain normal, preserving for some time a certain susceptibility because of which minor manifestations may reappear. But finally functional balance may be restored and may last until the coming of old age. The exact symptomatology of climacteric hyperthyroidism will be explained in detail elsewhere in this book.

Climacteric Hypothyroidism

The *hypothyroid reaction* of the critical age, I have already said, is much less frequent than the hyperthyroid, although not, therefore, less interesting clinically. Like hyperthyroidism, climacteric hypothyroidism generally occurs in women who previously presented symptoms manifesting a *hypothyroid temperament*, a tendency to obesity, lymphatic aspect, insufficient menses and genital powers, scanty hair and eyebrows, calm disposition, sensitiveness to cold, dry skin, and so forth. In these cases, the menopause appears early and causes an accentuation of all these signs up to pathologic limits, even myxedema itself. All writers give the menopause as one of the moments of election for the onset of myxedema. I have seen some examples in the last few years, which had not been readily recognized and of which I shall speak again in the chapter on the *clinical forms of pathologic menopause*. Curschman²⁵ and Deusch²⁶ have given particular attention to this question.

²⁴Brooks: Physiological hyperthyroidism, *Endocrinology*, 1921, p. 177.

²⁵Curschman: Klimax und Myxoedem. *Zeits. f. d. ges. Neurol. und Psychiat.*, 1918, No. 41.

²⁶Deusch: Klimax und Myxoedem. *München. med. Wchnschr.*, 1919, page 589.

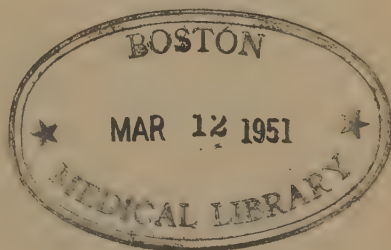
I stress the point that even among women who previously were of the hypothyroid type and who at the close of the menopause seem to be even more so, a hyperthyroid reaction, perhaps very mild, is frequently observed in the first part of the crisis. Such symptoms of hyperthyroidism as tachycardia, palpitation and a certain nervousness are mixed in with the usual ones of hypothyroidism for some time, giving rise to an equivocal picture which corresponds to the descriptions of *thyroid instability* which will be considered later.

Thyroid Instability of the Critical Age

This *thyroid instability* in other cases is the constant type of climacteric reaction of the thyroid. The most typical, most complete cases of thyroid instability, as described by Levi and Rothschild,²⁷ occur in menopausal women.

In this mixed syndrome, as I said, there appear the symptoms of thyroid insufficiency along with those of hyperfunction. But more striking than the mere mingling of these two types of symptoms is the *variability* or the *instability* of the thyroid manifestations, that is, the rapid succession of hyper- and hypofunctional symptoms which characterizes this state. Still, as De Quervain²⁸ observed, the manifestations of hyperthyroid type, such as tachycardia, palpitation and vasomotor upsets, almost always predominate.

When considering the treatment of *arthritis in the critical age* I shall speak again of this *thyroid instability*, taking up the pathogenic relations which unite both states.



²⁷Levi and Rothschild: See note (1), page 38

²⁸De Quervain: *Le Goitré*. Geneva, 1923.

CHAPTER IV

THE SUPRARENAL FACTOR

Do the Suprarenal Glands Intervene in Climacteric Symptomatology?

Debate on this point stirs up so many problems—problems which are perhaps the most passionately discussed in present-day medicine—that I shall give only a preliminary résumé of the question in order that the reader who may not be familiar with the discussion may have some basis for his own opinion. Suprarenal physiology was precisely the point of origin in the revolutionary revision of endocrinology initiated by Gley and his adherents. It is scarcely possible to refrain from taking sides in the debate which rages furiously.

The suprarenal glands consist of *two kinds of tissue, medullar and cortical*. Until Gley's work appeared it was accepted as indubitable that the medullar substance secreted adrenalin, a hormone capable of influencing the sympathetic nervous system, blood pressure and carbohydrate metabolism. The cortical substance was regarded as taking part, perhaps, in antitoxic processes, due to cholesterin and other lipoids, and in the complex mechanism of sexual morphology, since cortical tumors coincide with the syndromes of pseudohermaphroditism and virilism in adult women. Thus, everything invited one to the belief that a good part of the symptomatology of the climacteric was of hypersuprarenal pathogenesis. In fact, this was my opinion in the first edition of this book. The hypertension and the tendency to hyperglycemia and glycosuria, so frequent in this age, were easily explained by the medullar hyperfunction. There were, indeed, hyperadrenalin syndromes. And the inversive tendency, the virile appearance so common in menopausal women, was explained in its turn by the cortical hyperfunction. Let us see calmly what remains of this theory.

The Present Controversy on the Physiologic Rôle of Adrenalin

The entire first part of this theory is now denied by Gley, that is, the part relating to the existence of hypertension and hyperadrenalinemic hyperglycemia-glycosuria.^{1, 2} Gley contends that adrenalin is not a true hormone and therefore physiologic adrenalinemia does not exist. Chiefly through the aid of American physiologists, like Stewart and Rogoff, Hoskins, Houssay and others, Gley's antiadrenalin viewpoint has been warmly adopted

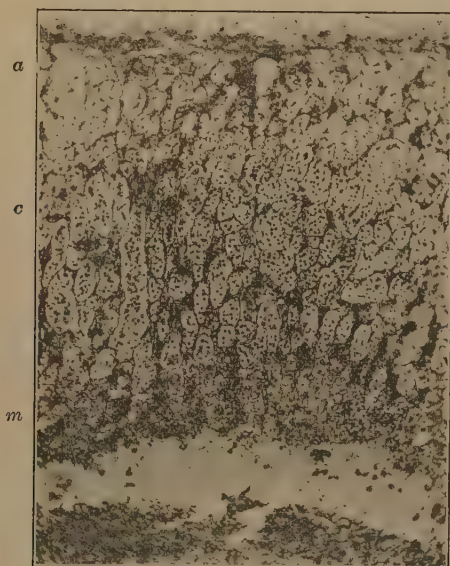


Fig. 4.—*Normal suprarenal gland: a*, periglandular adipose tissue; *c*, cortical substance; *m*, medullar substance, with an artificial cavity in the center. (Calandre, Banus.)

by a large part of the scientific world. Thus not only in controversial articles but also in texts³ do we read that this action is merely pharmicodynamic, and that the assumed physiologic action of adrenalin on vascular pressure and on the rest of the body is purely illusionary.

¹Gley: *Quatre leçons sur les sécrétions internes*, Paris, 1920.

²Gley: *La physiologie des surrénales et la sécrétion d'adrenaline*, *Revue de Médecine*, 1923, No. 4.

³Hoskins: *Relation of the Suprarenal Glands to the Circulation*, *Endocrinology and Metabolism*, B.H. and M., ii, New York, 1922.

Without entering into the details of the problem here I *hasten to state my complete belief in the physiologic rôle of adrenalin*. Understand it is possible that I may change my opinion later. Clinging doggedly to old ideas is the most efficacious factor leading to stagnation. But at present I regard as unscientific the "physiologists'" attempts to discredit, by means of a few doubtful experiments, conceptions which have been acquired through years of patient clinical and physiologic investigation. Let us examine the question briefly.

Writers who deny the existence of physiologic adrenalinemia rely principally on two facts. First, scrupulous experiments show that after bilateral extirpation of the suprarenal glands arterial pressure is not lowered, while, on the other hand, asphyxial hypertensions (emotions, etc.) are produced which had been attributed to hypersecretion of the suprarenal medulla. Second, it is impossible to demonstrate the existence of adrenalin except in very small amounts in the blood of veins near the suprarenal vessels and a little in the arterial blood. The objection can be raised against the first argument that extirpation of both suprarenals does not necessarily mean the total ablation of the source of adrenalin since a more or less abundant quantity of extracapsular chromaffin tissue exists. Many investigators attest to the abundance of this extracapsular tissue which escapes extirpation. Thus the argument is not closed. I have had personal experience with this fact in the human species. Moreover, I would cite the words of a physiologist, doubly authoritative since he is an eminent investigator and sides with the anti-adrenalin faction. I refer to Houssay who said recently after stating that the suprarenal medulla is not indispensable to life: "*By this I do not mean to say that chromaffin substance is not, since it is known that there is relatively more extracapsular chromaffin tissue (that is of medullar type which produces adrenalin) than extracapsular cortical tissue. But extirpation of the suprarenals reduces the amount of the latter more than that of the former proportionately.*"⁴ That is to say, there is an extracapsular chromaffin tissue of sufficient physiologic capacity to vitiate the

⁴Houssay: Importancia respectiva de la corteza y de la medula suprarrenal. In Libro en honor de Cajal. Madrid, 1922. This monograph is a summary of the numerous articles published on this point by the author.

value of the results of extirpation of both glands. As for the other argument, that circulating adrenalin cannot be demonstrated, it has no value. Our methods at present are not sufficiently precise to make such negative data worth while. No one has yet demonstrated the thyroid or the ovarian hormones in the arterial or in the venous blood. Yet no one doubts their existence.

The antiadrenalin theory, based upon such negligible experimental data, has recently been the object of a rude attack through the experiments of Tournade and Chabrol.⁵ Gley himself pronounced these tests "exquisite."⁶ Tournade and Chabrol anastomosed the suprarenal vein of one dog, *A*, with the jugular of another dog, *B*. After excitation of the dog *A*'s spleen, it was observed that the arterial pressure of the dog *B* was raised. This phenomena is only explicable by a humoral action transmitted from *A* to *B*, that is to say, by the passage to *B* of the adrenalin secreted by *A*'s suprarenal glands excited by way of the spleen.

Moreover, aside from this experimental controversy, the anti-adrenalin theory *has ever erred gravely by ignoring clinical results*. To be sure it is, on occasion, difficult and daring to deduce physiologic conclusions from clinical data. But this fault of lightness is not comparable to that of impertinence, so common in much contemporaneous physiology, which is guilty of completely ignoring clinical and anatomicopathologic results of unquestionably demonstrative value. This is the case with suprarenal insufficiency. Will the physiologists say nothing of the hundreds of cases of Addison's disease, with its clearly marked syndrome, so typical, so constant and its invariable lesion? If one of the most characteristic symptoms of this disease is *an early hypotension of an intensity found in no other pathologic process* save in the hours preceding death, and if the lesion so destroys the suprarenal medulla, elaborator of adrenalin, that only very small parts or none at all are found at autopsy, should we not associate the serious hypotension with the *chronic* lack of adrenalin? I have asked elsewhere and I ask again, "Have we, for example, discovered the cerebral localizations with a like

⁵Tournade and Chabrol: L'adrenalinemie, *Revue de Medecine*, 1923, No. 4

⁶Gley: *Op. cit.*, note (1), page 51.

criterion of rigid interpretation?" Gley himself at an autopsy—one of Sergeant's cases of Addison's disease—recently wavered⁷ from the point of view he had so obstinately maintained before he had the opportunity of comparing experimental results with those of the clinic supplemented by postmortem examination.

Nor is this all. Adrenalin, besides its hypertensive action, has a hyperglycemic action which is as constant and clear. In chronic suprarenal insufficiency, Addison's disease, hypoglycemia appears *parallel to the arterial hypotension*. Porges⁸ demonstrated this and my associates, Carrasco and Soler,⁹ recently confirmed it in a high percentage of a large series of cases—that is, large considering the rarity of the disease.¹⁰ Looking at these facts calmly, can we continue saying that adrenalinic hypertension and hyperglycemia are merely pharmacodynamic occurrences?^{11, 12}

Are There Clinical States of Hyperadrenalinemia?

I continue, then, to believe in the physiologic action of adrenalin and in the pathologic repercussion of its altered secretions. The disturbances due to suprarenal insufficiency are well known—Addison's disease and the acute form of suprarenal insufficiency—and *although we know that in these the lack of adrenalin is not the sole factor*, the phenomenon being much more complex, yet hypoadrenalinemia plays the chief, the indispensable rôle, as we shall see presently. *In the present state of our knowledge on this point, the opposite syndrome, the hyperfunctional, has*

⁷Sergeant and Ourv: Quelques reflexions sur l'insuffisance surrenale aigue, Revue Francaise d'Endocrinologie, 1923, No. 1.

⁸Porges: Ueber Hypoglykämie bei Morbus Addisonii, sowie bei nebennierenlosen Hunden, Ztschr. f. klin. Med., 1909, Bd. 69.

⁹Marañón, Carrasco and Soler: Sobre la glucemia en la enfermedad de Addison, Bol. de la Soc. Esp. de Biología, November, 1923.

¹⁰Parallel to these clinical facts, experimental results reported by many writers confirm physiologic suprarenal intervention in the regulation of carbohydrate metabolism. The experiments made by Negrin and his school should be noted particularly. These are summarized in El papel de los adrenes en las glucosurias de origen bulbar, in Libro en honor de Cajal, Vol. II, Madrid, 1922. The "antiadrenalinic" physiologists completely overlook this entire class of important findings. In Gley's articles there is not a single allusion to Negrin's work.

¹¹I cannot go into greater detail here. I fully considered this point in my book Problemas actuales de la doctrina de las secreciones internas. Madrid, 1922. Moreover, read the admirable articles by Pende¹².

¹²Pende: La critica demolitrice di alcuni moderni fisiologi sulla fisiopatologia surrenale. Endocrinologia e Patologia Costituzionale (Rome), 1922, 1.

Pende: Has Adrenin Any Physiological Value in the Organism? New York Med. Jour., 1923, cxviii.

no scientific entity. Therefore, we may no longer speak of "hypertension" and "diabetes" as due to hyperadrenalinemia as I and other writers did for many years. The suggestions that conduce to this hypothesis are, when examined, irresistible. If the pathologic destruction of the suprarenal medulla produces hypotension and hypoglycemia, an opposite state, hyperplasia with hyperadrenalinemia ought to lead to contrary, clinical results, that is to say, hypertension and hyperglycemia and glycosuria. But careful observation shows us, first, that this anatomic state of medullar hyperplasia has not yet been proved in a sufficient and significant number of autopsies; and second, that arterial hypertension—in general terms—and diabetes are phenomena of a complexity incompatible with the simple explanation of hyperadrenalinemia.

May we completely overlook the possibility that these states of hyperadrenalinemia do exist and that they have an influence on the mechanism of the production of some states of hypertension and glycosuria? Clearly not, theoretically. There are no positive proofs that hyperadrenalinemia exists, but neither is there any reason to deny that the suprarenals, like the other glands, may react under pathologic stimuli by hyperfunction in some cases, as in others they react by hypofunction, Addison's disease.

Admitting this possibility climacteric symptomatology, at least in a goodly number of cases, adjusts itself to theoretic hyperadrenalinemia as to nothing else. Later, in the chapters devoted to the symptomatology, we shall see that frequently the onset of involutional manifestations coincides with an increase of arterial tension. Although some writers have denied this fact, its proof is so abundant it is impossible to doubt. And aside from its frequency this hypertension is generally transitory, disappearing some months or years later when the crisis is past, thus refuting the conjecture that, as really occurs in some cases, there was a senile hypertension due to premature sclerosis. I have proved the transitoriness of climacteric hypertension in a number of patients under observation for several years, and am thus assured that I speak without flagrant error. Moreover, climacteric hypertension varies from time to time and is greatly influenced by emotion. These facts set it off from the fixed hypertension due to lesions of the circulatory or renal system. Does

not all this invite us to admit a state of functional hypertonia of the circulatory system, in the mechanism of which there intervenes the sensitizing of the sympathetic system by the adrenalin which is secreted with abnormal frequency and abundance?

But further, in many of these cases of hypertension, as I have shown, coincident with Kylin and others,¹³ the hypertension is accompanied by hyperglycemia, or by alimentary glycosuria. Sometimes it is the precursor of a diabetic state, properly so-called, at first transitory and later permanent. In various cases carefully and extensively observed during some years I have been able to make out this succession of stages:

Hypertension with hyperglycemia.

Intermittent glycosuria.

Definite diabetes.

The hyperadrenalin hypothesis is brought to mind also in these cases to explain the state of "hypersensibility" in the sympathetic system and in the regular mechanism of carbohydrate metabolism, although not as the sole and permanent cause of diabetes. *Therefore, I do not hold that the assumed hyperadrenalinemia of the climacteric is "the cause" of the hypertension and of the diabetic tendency proper to this age; but that it may have an exquisitely "sensitizing influence" on the vegetative system in the production of these manifestations in the peculiar clinical form which they adopt in this period of life.*

Menopause and Suprarenal Cortex

So much for the medullar portion of the suprarenal. *As for the cortical part, as I have said, climacteric symptomatology is well adapted to the hypothesis of its possible hyperfunction. Indeed, as all writers admit, the hypercortical syndrome is manifested clinically by the development of the secondary masculine sex characteristics when it concerns women (the most frequent case, and the most interesting for our present study), and by the accentuation of the masculine characteristics in the case of men. It appears that the suprarenal cortex is capable of providing a*

¹³See the literature in the chapter devoted to the Circulatory Symptoms of the Climacteric.

humoral impulse which stimulates the appearance of the secondary characteristics of the male sex. This impulse remains latent in woman all her life, but it is not dead, because it can be revived through pathologic circumstances. In the man this hormone acts with varying intensity, according to different physiologic or pathologic circumstances.

When these pathologic conditions are present—I refer now only to women—they produce a revivification of masculine morphologic and functional signs, giving rise to the clinical form well described by Gallais with the name *genitosuprarenal syndrome*.¹⁴ The clinical appearance differs according to the stage of life wherein the syndrome appears. When it occurs in the adult, the age of greatest interest to us, the syndrome assumes the type called *suprarenal virilism*. The menses cease. The character alters tending to masculinity. The general morphologic changes are those of adiposity. The voice takes on a heavy, masculine tone and lastly, abundant ectopic hair appears on various parts of the body, as on the trunk, chin or upper lip. The dependence of this curious symptomatology upon adenomatous hypertrophy of suprarenal cortical tissue appears certain. In fact in one case, Bovin,¹⁵ this cortical neoformation was surgically extirpated, whereupon the signs of virilism disappeared and feminine morphology was restored.

These cases of *pathologic virilism* are exceptional. They concern extraordinary anomalies, many of which are celebrated monsters. *But are not these very changes which I have enumerated, in lesser degree the same which we see so often in menopausal women?* Very frequently after the critical years, when the menses have ceased, the woman grows corpulent, a state accompanied by a certain amount of localized adiposity the characteristics of which I shall take up presently. At the same time the character changes. Not infrequently sweet, feminine ways are lost. She become aggressive. The voice may become rough. A light or heavy tracing of a mustache may appear, with more or less down on the chin and perhaps on the limbs and trunk. This transformation, the popular idea of the “mother-in-law,” is doubtless

¹⁴Gallais: Le syndrome genito-surrenal, Paris, 1914.

¹⁵Bovin: Les tumeurs hypernephroïdes primitives des organes genitaux féminins, Ref. en Sem. Medical, 1910.

a minor grade of the monstrous virilism, which was referred to above, and may, therefore, be interpreted as the result of a climacteric suprarenal cortical hypertrophy. Admitting, then, that normally the extinction of ovarian secretion, guardian of the feminine secondary sex characteristics, leaves the suprarenal cortical secretion, stimulator of the masculine sex characteristics, without a curb, the masculine signs then appear in greater or less degree according to the given case.

I do not wish to overlook the fact that latterly the participation of the suprarenal cortex in this symptomatology has been subjected—like so many other points in endocrinology—to critical revision.

Indeed, different writers have proved by autopsies in cases of typical virilism that the suprarenal cortex may not be hypertrophied. I recently dissected the cadaver of a woman of sixty, who died in our clinic of cancer of the stomach, in whom the virile syndrome was marked, abundant mustache and down over the whole face, arms, and legs. The cortex of the suprarenals not only was not hypertrophied, but was well atrophied, especially with relation to the medullar substance, which was very thick. Histologic examination by Prof. Del Rio confirmed the absence of evidence of hyperfunction in the cortex. The ovaries presented the characteristics of senile sclerosis, perhaps more pronounced than corresponded to her age. Krabbe¹⁶ in view of these vegetative cases offers the hypothesis that sometimes these supposed tumors of the suprarenal cortex may be in reality tumors developed at the expense of the testicular cells, remnants of the embryonic bisexual state. It is worth the trouble to consider this suggestion, which is logical. Recently W. H. Schultze¹⁷ maintained that the hypophysis intervenes in these appearances of hair or “secondary piliosis.” Certainly this topic should be subjected to clinical and histologic revision in the future.

¹⁶Krabbe: The Relation Between the Adrenal Cortex and Sexual Development, New York Med. Jour., July, 1922.

¹⁷Schultze, W. H.: La pilosis secundaria de la mujer, como sintoma de trastorno hipofisario. Arc. de Medicina, Cirugia y Especialidades, Madrid, 1924, xiv. This is a confused study which, nevertheless, will be taken into account later. At this time I cannot give a critique of Schultze's statements.

In brief, the interpretation of certain clinical manifestations lead—as we have seen—to an admission of a state of total hyperfunction of the suprarenal organs in this age. Some anatomic and experimental data appear to strengthen this supposition which I repeat is set forth here with every reservation.

Condition of the Suprarenals in the Critical Age

Examination of the suprarenals in different periods of life teaches us in the first place that these glands do not follow, as do the most of the other organs, an evolution which may be represented by a curve ascending from birth to reach its greatest height in the maturity of life, and leaving which it begins a progressive descent, parallel to the whole decline of the organism, both ending in death. On the contrary, we see that in the course of life the anatomic development and the functional activity of the suprarenals undergo various fluctuations independent of the general evolutionary curve. These organs increase in weight after the fiftieth year according to my observations, excluding as far as possible errors due to changes stamped upon them by the disease producing death. I have systematically examined the suprarenal capsules in many cadavers and the rule is that, after fifty, these organs, previously small, of poor consistency and not very thick, are progressively changed. This is tactually appreciable at autopsy. The organs are thicker and little or not at all friable. When examined macroscopically, the difference between a suprarenal in youth and that in a man who has passed maturity is easily observed. In the former the medullar substance is scarcely more than a thick line, encompassed by the smooth yellow one constituting the cortex, both separated by the vague and delicate line of the pigmented zone. In the suprarenals of a cadaver of more than forty years, section of the gland shows a thick, medullar substance accumulated in broad islands surrounding the vessels, the cortex being folded in true convolutions about the medulla. We cannot be precise as to the proportion of cases wherein this transformation occurs, nor its rate of progress nor any of its chronologic details. Nor can we determine the exact limits which separate physiologic hypertrophy from the pathologic hyperplastic processes which

have been described as occurring in this age. But any one who does much postmortem investigation in the suprarenal region will be surprised at the fact to which I have just called attention and which certainly indicates *that the suprarenal function, far from weakening when the whole organism declines, experiences an increase of its activity in these years of the crisis.* Husnot¹⁸ and Sabrazes and Husnot¹⁹ have made a special study of the macroscopic characteristics and the histology of the suprarenal glands in the different stages of life, confirming an undeniable



Fig. 5.—Macroscopic aspect of sections of normal and pathologic suprarenal gland (Sezary): *a*, normal gland; *b*, gland with hypertrophy of the cortex which appears folded upon itself, as is likely to be observed in the period of declination; *c*, suprarenal gland in a state of hypofunction.

medullar and cortical hyperplasia, a true multiple adenomatosis, which develops at the time that the organism, as a whole, declines. The observations of Sabrazes and Husnot refer almost always to subjects of more than seventy years. But, I repeat, my impression is that the suprarenal hyperplasia begins long before, probably coincident with the period of the involution.

¹⁸Husnot: *Recherches sur l'évolution histologique de la glande surrénale chez l'homme*, Paris, 1905.

¹⁹Sabrazes and Husnot: *Senilité et hypertrophie de surrenales*. *Rev. Franc. d'Endocrinologie*. Ann. I, No. 1, 1923.

Condition of the Suprarenals in the Castrated Organism

They also confirm, on one side, my postmortem observations, and, on the other, the fact that climacteric symptomatology coincides with the "theoretic syndrome of hypersuprarenalism." Finally, study of the behavior of the suprarenals after castration tells the same story, except, of course, sudden suppression of the genital function in an animal produces states which are not exactly comparable to the complex crisis of spontaneous menopause in women. Ciaccio²⁰ found a hypertrophy of cortical substance in castrated animals, up to double normal weight and the experiments of Theodosiew,²¹ Marrassini,²² Schenck²³ and others lead to the same conclusion. The hyperplastic signs appear not only in the cortex but also in the medullar substance as Schenck²⁴ and Cecca²⁵ have demonstrated.

I have confirmed these findings in castrated rabbits. On killing the animal in from four to twelve months after castration the increase in size of the suprarenals is apparent at a mere glance compared to those of uncastrated animals of the same age. The weight confirms this increase and section demonstrates the hyperplasia of the normally narrow medullar substance and that the cortex, always thick in the rabbit, in the castrate becomes veritably exuberant, adenomatous.

Adrenalinic Glycosuria in the Menopause and in Castration

The results of experimental investigation coincide with these anatomic data. The experiments show that adrenalinic glycosuria is produced in castrates by smaller doses of adrenalin than are necessary in the uncastrated or in healthy nonmenopausal

²⁰Ciaccio: Sui processi secretorii della corteccia surrenale. *Anat. Anzegl.* Bd. xxviii, 1906.

²¹Theodosiew: Hypertrophie der Nebennieren nach Entfernung der Eierstocke. Ref. in *Biophysikalische Central*, Bd. ii, 1907.

²²Marrassini: Sopra le modificazioni che si hanno nelle capsule surrenali in rapporto con alcune variazioni della funzioni genitale, *Lo Sperimentale*, ix, 1906.

²³Schenck: Ueber die Veränderungen der Nebennieren nach Kastration, *Beit. zur klin. Chirurg.* Bd. lxxvii, 1910.

²⁴Schenck: Kastration und Adrenalinegehalt der Nebennieren, *Arch. f. exper. Path. u. Pharmacol.* Bd. lxiv, 1911.

²⁵Cecca: Ovaire et surrenale. *Soc. med. de Boulogne*, 1904.

women. Cristofolletti²⁶ and I²⁷ have demonstrated this in the castrated woman, and Adler²⁸ and I in the menopausal woman. Adler observed (and I have confirmed this) that the other symptoms which injection of adrenalin produces—besides glycosuria—such as pallor, vasomotor disturbances and dizziness, are more marked in the climacteric woman than in the normal. Furthermore, the emotional reaction which I have described occurs; of 27 cases examined this was positive in fourteen.²⁹

Climacteric Hypercholesterinemia

The greater sensibility to adrenalin on the part of hypogenital individuals appears to lead us to accept medullar hyperplasia of the suprarenals. The theory of cortical hyperplasia has in its favor, aside from the above clinical data, the increase in circulating cholesterin. Indeed, according to Chauffard and Grigaut's group,^{30, 31} the suprarenal cortex is one of the principal sources of the cholesterin which circulates in the blood. Thus the amount of this hepatic cholesterin would be an index of corticosuprarenal function. I have accepted this idea with some reservations. Provisionally we may interpret variations of cholesterin as paralleling the functional state of the cortex of the suprarenal glands. Here are the facts on this point.

Neumann and Hermann³² discovered that in castrated women and in those who were traversing the climacteric and postclimacteric periods there exists in the blood an abnormally large quantity of lipid substance. I have determined the amount of cholesterin in the blood of a certain number of women in the

²⁶Cristofolletti: *Zur Pathogenese der Osteomalazie*. Gynäkologische Rundschau, 1908, v.

²⁷Marañón: Nota preliminar sobre la acción de los distintos extractos de órganos sobre el metabolismo hidrocarbonado, Bol. de la Soc. Esp. de Biología, 1914.

²⁸Adler, L.: *Zur Physiologie und Pathologie der Ovarialfunktion*, Arch. f. Gynäk., 1912, xcv.

²⁹Marañón: Contribución al estudio de la acción emotiva de la adrenalina, Libro en honor de Cajal, II, Madrid, 1922.

³⁰See a summary of the question in Grigaut's thesis: *Le cycle de la cholestérimie*, Paris, 1900; and in

³¹Guy Laroche: Capsules surrenales et cholestérine, Rev. Franc. d'Endocrinologie, 1923, i, No. 3.

³²Neumann and Hermann: Biologische Studien über die weibliche Keimdrüse, Wien. klin. Wchnschr., 1911, Falta assumes for the lipoidemia of menopausal women a directly genital origin—stating that he has proved it. See op. cit., note (16), page 19.

midst of the menopausal upset, obtaining figures higher than the average normal which certainly is lower than the 1.5 per cent claimed as being usual by Grigault and his followers. Clearly in these women it is difficult to eliminate other causes which, aside from the climacteric, may act on the quantity of the circulating cholesterin. Therefore, with Echauz, I have revised data previously obtained, subjecting it to critical analysis. But I believe that the existence of a hyperlipoidemia, or more exactly a hypercholesterinemia, may be accepted as an assured fact in the menopause. Let us now consider the pathogenesis of this phenomena.

Neumann and Hermann found that by injecting in a normal woman extracts of suprarenal gland or of hypophyseal gland, a clear, although transitory, hyperlipoidemia is produced. This led them to suspect that the menopausal hyperlipoidemia discovered might have its origin in the corticosuprarenal hypertrophy which, as we have just demonstrated, is developed in this period of life. Later they abandoned this hypothesis, because of theoretic assumption that the suprarenals do not turn their substances into the blood, and, for that reason, could not influence the amount of these lipoids which the blood stream contains.

Let me reiterate that my position here is one of watchful waiting, as to whether cholesterinemia is or is not the result of corticosuprarenal function. But let us recall the significant fact that the amount of cholesterin is increased in the menopause. I believe that no other explanation is more logical than that which relates it to the suprarenal hyperplasia normal in the climacteric.

Conclusion

In short, without being able to establish a basis of incontrovertible fact for my hypothesis, dispassionate examination of the clinical, anatomic and experimental data leads me to state, without fear of scientific heresy, that the suprarenal glands react in a hyperfunctional way in the climacteric period, and that this hyperfunctional state can be related, from the pathogenic point of view, to a part of the symptomatology of this age.

Climacteric Hyposuprarenalism

The contrary reaction, suprarenal insufficiency, is on the other hand extremely rare in the involutional period. Suprarenal insufficiency is an affection essentially youthful. Under the name *hypoadrenoovarian* syndrome, I have described³³ frequent association of the ovarian insufficiency of girls with more or less intense states of hyposuprarenalism. But rarely has this condition been observed arising in the menopause of normal women. What is likely to occur more frequently is that women previously afflicted with suprarenal insufficiency grow worse when the menopause occurs, which certainly is likely to be very easily and frankly pathologic if the gravity of her illness has permitted the woman to reach the age of the crisis, for death usually supervenes. If death does not occur, the symptoms of Addison's disease, such as asthenia, emaciation, melanoderma, hypotension and digestive disturbances are accentuated.

Later I shall speak of the pigmentations, either cutaneous or mucous, which appear in this age. Let me state that it would be erroneous to attribute them to suprarenal insufficiency. Their origin is clearly ovarian and no good clinician will become confused on this point.

³³Marañón: . Op. cit., note (4), page 26.

CHAPTER V

THE HYPOPHYSEAL FACTOR

Pancreas and Menopause

In the preceding chapters we have studied the most frequent elements of the *menopausal* crisis—that is, ovarian insufficiency, hyperthyroidism and hypersuprarenalism. Is the crisis limited to these disturbances? Of the remaining glands the pineal and the thymus have been inactive for some time—since puberty. Hence there remain for consideration only the pancreas and the hypophysis. The pancreas follows the general law, tending to weaken on approaching the critical age, thus favoring the appearance of glycosuric states, so frequent in these years. Otherwise its influence is without special characteristics.

Climacteric Hypopituitarism

With regard to the hypophysis, I have already explained my reasons for not accepting Culbertson's hypothesis,¹ according to which this gland functions excessively, collaborating with the suprarenal hyperfunction in the production of the climacteric hypertension. On the contrary, all the indications are that the extinction of sexual activity is accompanied or preceded by a parallel suppression of the hypophyseal activity. This fact of climacteric hypopituitarism is doubly curious, for here just the opposite state develops from that appearing in the thyroid and the suprarenals—according to the argument in the preceding chapters. In the genital crisis occurring in youth (puberty) hyperfunctional reaction of the hypophysis is frequent, and in the genital crisis of maturity (menopause) hypofunction is the rule. We often see girls in whom at puberty the menses are established with difficulty, who grow rapidly, presenting an un-

¹Culbertson: Op. cit., note (28), page 21. Schultze's ideas note (17); page 58 on the hypophyseal origin of feminine pillosis are also in favor of a hyperfunctional reaction of the hypophysis in the climacteric, since one of the phenomena of this age is the appearance of this hair. But I reiterate my reservations as to this hypothesis.

graceful appearance with disproportionate hands and feet and massive features. All these are signs of an energetic and disordered function of the hypophysis (*pubertal hyperpituitarism*). But in the menopause, as I have said, the rule is for symptoms of hypopituitary interpretation to appear—such as obesity and amenorrhea. The thyroid and the suprarenals react inversely to the pituitary. In puberty they frequently present hypofunctional syndromes associated with ovarian insufficiency while in the menopause they present the hyperfunctional.

Now hypophyseal insufficiency leaves scarcely any traces on the organism which has reached maturity. Consequently hypopituitary symptoms are not very ostensible in the menopause. [The experimental work which formed the basis for my views expressed in 1916 simply showed that vasomotor symptoms could be produced or exaggerated in women of the hypertensive (climacteric) type by injections of either pituitrin or supra-renal. These observations have been repeatedly confirmed since. As a result I then thought that the instability on the part of the pituitary, suprarenal and thyroid glands was the result of ovarian insufficiency, and that this instability was expressed often by evidences of decreased function, again by evidences of increased function, but that this increase or decrease was always relative, never absolute. The presentation here offered by the author would show that with the hypophysis this functional unevenness (instability) is more often expressed by evidences of insufficiency. My idea then was that at no time would there be a positive increased function, but that this might appear to be the case if the other glands involved were exhibiting insufficiency at a time when the hypophysis was, as it were, standing still. The author's argument here goes far to clear up this matter, so complicated and so difficult to express concisely.—C. C.] Indeed, the hypopituitarism is revealed especially by two symptoms—obesity and the weakening of the genital function. This syndrome, described by Fröhlich as *dystrophia-adiposo genitalis*, is very striking when it occurs in youth. Then there is a typical atrophy of the genital organs and the obesity, of eunuchoid type, gives to the general morphology unmistakable characteristics.

On the other hand, when hypopituitarism occurs in the adult, genital atrophy is not presented and there is only frigidity and impotence in the male and menstrual suppression in the female—phenomena which have much less significance in this period of life. As for the obesity, its characteristics are less showy during these involutional years. It is doubtless legitimate to assume that hypophyseal insufficiency participates in sexual extinction and in the menopausal increase in weight.² [In my opinion these symptoms are evident but usually not recognized as such by the physician who thinks of the climacteric in terms only of vasomotor disturbances characterizing the hypertensive type. The hypotensive patient complains more of weakness and malaise, loss of tone and ambition, even of loss of memory, more than she does of menstrual suppression and sexual frigidity. This asthenia often amounts to a real distress and is exaggerated by the fear of losing her mind. The whole picture suggests but falls short of myxedema.—C. C.]

Hypophyseal Cachexia in the Menopause

We now know that while mild hypophyseal insufficiency produces states of obesity, when this functional deficiency is very great, the obesity changes into a rapid and progressive emaciation—true cachexia. Pende³ and Simmonds⁴ very properly call attention to the scant interest writers, and I include myself among them, have paid to this manifestation of hypopituitarism.—*hypophyseal cachexia*. Nevertheless its existence is indubitable. As we shall see presently, I believe that grave hypopituitarism is the explanation of those cases in which, after a very active genital life—often repeated pregnancies—women grow thin and show rapid and extreme ageing. They may become truly ca-

²I cannot enter here into the recent discussion as to whether Fröhlich's adiposogenital syndrome is, indeed, due to hypophyseal insufficiency or to a lesion of the parahypophyseal vegetative centers; or, better, to a collaboration of both factors, the endocrine and the nervous. I recently explained my opinion as being favorable to this eclectic hypothesis. But I grant a greater value to the participation of the hypophysis, since clinical data of positive value demonstrate this. See a résumé of the question and of the facts personally collected in Marañón, Über die hypophysaire Fett-sucht, Deutsch. Arch. f. klin. Med., 1926, cli.

³Pende: Op. cit., note (17), page 19.

⁴Simmonds: Über Kachexie hypophysären Ursprungs, Deutsch. Med. Wehnschr., 1916, No. 7.

chectic in the absence of lesions to explain debility, no etiologic causes being apparent except the excessive multiparity. I have called this syndrome *climacteric senilism*, attributing a fundamental rôle to the hypophyseal exhaustion.

Diabetes Insipidus and Menopause

In closing there should be mentioned a manifestation which recent studies, among them my own,⁵ have demonstrated that,



Fig. 6.—Acromegaly appearing on the occasion of a premature menopause (thirty-nine years). Large hypophyseal tumor, with progressive hemianopsia. In Fig. 7 the beginning of the patient's hyperpituitary predisposition may be seen. (Personal case.)

at least in a group of cases, diabetes insipidus is due to an insufficiency of the posterior lobe of the hypophysis. *This syndrome is also observed in the climacteric or preclimacteric age*

⁵Marañón: Nuevas orientaciones sobre la patogenia y tratamiento de la diabetes insípida. Madrid, 1920, Ibid. Diabetes insipidus as a hypopituitary syndrome. Endocrinology, Los Angeles, 1921.

although more rarely than in earlier years. Yet several cases have been reported which developed between thirty-five and forty years. Transitory polyurias, if not true diabetes insipidus, are observed in many menopausal women. This symptom, which is generally attributed to nervous states may be interpreted as a manifestation of menopausal hypopituitarism. I have published two reports—Cases 23 and 24 in the volume just cited—to which I add a third, now even more typical.

CASE 1.—A. M. de H., fifty years old. Iritis, without syphilitic symptoms, and negative Wassermann reaction; malaria. *Present state:* at forty-nine



Fig. 7.—The same patient as in Fig. 6 at twenty-seven years of age. In perfect health, yet enlargement of the features may be noted, precursor of acromegaly.

climacteric disturbances began—severe metrorrhagia and dyspnea. *Coincident* with this, thirst appeared and polyuria, amounting to 12 liters. No sugar or albumin; specific gravity of urine 1.002, with a proportionate dilution of normal elements. Six months later this acute syndrome disappeared except that polyuria persisted, amounting to 3 liters, with a specific gravity of 1.002. Blood pressure* showed a hypertension (21-10 mm.) and increase of the second aortic tone. She gained six kilograms in weight. At present there is still occasionally a scanty menstruation.

*Translator's note: See page 142 for author's comment on blood pressure readings. He considers every figure above 9 abnormal.

I have consulted several competent persons who assure me they know of no way to transfer the blood-pressure readings over into our figures.

In this case, as in the others, perhaps more marked in this one, the coincidental appearance of the polyuria and the climacteric and the short duration of the former impel one to connect both states pathogenetically, bearing in mind that this is also the age wherein polyurias due to renal sclerosis begin. Aside from this possibility, hypophyseal insufficiency seems the most logical ex-



Fig. 8.—Hyperpituitary reaction of the climacteric. There were no focal symptoms and x-rays showed a sella turcica discretely enlarged. (Personal case.)

planation, especially when, as in my cases, the polyuria coincides with an increase in weight.

I pass over the other opinion that the hypophysis does not take part in the production of the polyuria, but that the latter is due to a lesion in the neighboring nerve centers. Roussy and Camus,⁶

⁶Camus and Roussy: *Experimental Researches on the Pituitary Body*. Endocrinology, 1920. These writers have published a multitude of notes and monographs on the question. See also their report to the III Reunion Neurologique Internationale, Paris, 1922. *Revue Neurologique*, 1922.

Houssay⁷ and others adhere to this opinion. But this is not the place to consider these contrary views.^{8, 9}



Fig. 9.—The same patient as in Fig. 8, fifteen years earlier, entirely normal.

⁷Houssay: This writer and his collaborators have published a great number of articles with regard to the rôle of the hypophysis in polyuria. See, as summary, Houssay, Galan and Negrete: Action des extraits hypophysaires sur la diurèse chez les chiens et les lapins. *Compt. rend. de la Soc. de Biol.*, 1920, lxxxiii.

⁸Among the adherents of the hypophyseal theory of diabetes insipidus, see Schiff: *Patologia de la hipofisis*, Edit. Paracelso, Madrid, 1923. A summary giving both sides of the question in ⁹.

⁹Froment: Rapport sur les syndromes hypophysaires. III Reun. Neurol. Intern. *Revue Neurologique*, 1922.

Climacteric Acromegaly

Although in the climacteric, hypophyseal hypofunction, as we have seen, is the rule, there are nevertheless cases of evident opposite reaction—hyperpituitarism. Many writers have described cases of acromegaly which began at the menopause and I have seen some since the publication of the first edition of this book. Nonetheless, I believe they scarcely merit the name “climacteric acromegaly.” At least the cases I have seen concerned women with an evident previous acromegalic predisposition, in whom the menopause only aggravated a previous clinical state. (Fig. 6.)

Occasionally the acromegalic syndrome is not clearly developed but only suggested—a coarsening but not excessive increase in the features and limbs. This, nevertheless, is sufficiently expressive so that a diagnosis of hyperfunction of the hypophysis may be made, as occurred in the case shown in Fig. 8.

CHAPTER VI

VEGETATIVE NERVOUS SYSTEM AND CLIMACTERIC

Anatomic Physiologic Outline of the Vegetative System

One of the basic ideas in endocrinology is the fundamental correlation between the vegetative nervous system and the glands of internal secretion. Here, too, I must briefly review the question, for the benefit of those of my readers who may not be in possession of these facts which are indispensable for exact comprehension of the following pages.*

The vegetative nervous system consists of two parts: *parasympathetic and sympathetic*. The *parasympathetic* is divided in its turn into two parts—*craniobulbar* and *sacral*. The sympathetic portion, included between the two parasympathetic portions mentioned, corresponds to the dorsolumbar region (see diagram). The *upper centers* of both lie along the cerebrospinal axis—the striated body, mesencephalon (periventricular nucleus, Luy's body, tuber cinereum, the black substance), medulla oblongata, cerebellum. From these centers *preganglionic bundles* go out converging into *ganglions*. The cells of these ganglions serve as the system's interrupting apparatus. From these ganglions new fibers emerge constituting the *postganglionic bundles*, which, in the form of nerves, are distributed through the visceral system.

*In this respect consult the following publications: ¹⁻¹⁴

¹Castellino and Pende: *Patologia del simpatico*, Milan, 1915.

²Brown: *The Sympathetic Nervous System in Disease*, London, 1920.

³Pottenger: *Symptoms of Visceral Disease*, C. V. Mosby, Co., St. Louis, 1919.

⁴Guillaume: *Le sympathique et les systèmes associés*, Paris, 1920.

⁵Müller: *Das vegetative Nervensystem*, Berlin, 1920.

⁶Novoa Santos: *Manual de Patologia general*, second edition, Santiago, 1922.

⁷Annes Dias: *Licções de Clinica Medica*, Porto Alegre, 1922.

⁸Guardia: *La clinica del simpatico y parasimpatica*, Paris, 1922.

⁹Kurt Dresel: *Erkrankungen des vegetativen Nervensystem*, in *Spez. Pathol. und Therap.*, by Kraus und Brughes, 1922, x.

¹⁰Escudero: *Lecciones de Clinica Medica*, Buenos Aires, 1923.

¹¹Laignel-Lavastine: *Pathologie du Sympathique*, Paris, 1924.

¹²Perrin and Hanns: *L'influence reciproque et l'action du sympathique et des sécrétions internes en pathologie*, *Rev. Franc. d'Endocrinologie*, December, 1923, No. 5.

¹³Castex: *Patologia del simpatico*, Buenos Aires, 1926.

¹⁴Bonilla: *Correlacion funcional entre el sistema nervioso vegetativo y las glandulas endocrinas*, Madrid, 1927.

(a) The *parasympathetic system*, consists, as I have said, of two parts—*craniobulbar* and *sacral*. The nerves of the *craniobulbar portion* are joined to the tympanic nerve, ocularmotor, etc. But its principal element is the vagus nerve, of such physiologic consequence (although it does not do much) that it has given its name to all this parasympathetic part of the vegetative nervous system. Even today one reads, at least in clinical descriptions, of the “vagus system” as opposed to the “sympathetic system.” Let us make clear, then, that the vagus is *only a part*, although the most important, of all the parasympathetic system.

The *sacral* portion is joined to the pelvic nerves, which are distributed through the bladder and rectum.

(b) The anatomy of the *sympathetic or dorsolumbar system* is well understood, with its intercommunications, its two longitudinal cords and sympathetic nerves, of extensive visceral distribution.

The interruptor ganglions are very distinct for each part of the vegetative system. The accompanying diagram gives an elemental idea of them and of all nerve distribution, better than would a long written description.

Vegetative Symptomatology. Its Indefiniteness

The *symptomatology* of the vegetative system is, in general, obscure—not so much because of the slight clinical entity of its manifestations as because of the fact that these manifestations are almost always associated with other well-defined clinical symptoms—nervous, digestive, endocrine, circulatory—which absorb the interest in the clinical picture. Vegetative pathology is, then, a “second rank” pathology and when writers endeavor to systematize “vegetative syndromes” the artificiality of this attempt is plainly seen. “Vagotonia,” “sympathicotonia,” are not definite and isolated syndromes, but “pathologic fundamentals” which accompany many a multitude of diseases, from which, barring exceptions, it is impossible to separate them. For my part, I have never been able to diagnose vagotonia or sympathicotonia in any patient, only *whatever the disease might be*—hyperthyroidism, ovarian insufficiency, hyperchlorhydria, circula-

DIAGRAM OF THE VEGETATIVE NERVOUS SYSTEM ACCORDING TO BROWN

Parasympathetic

Sympathetic

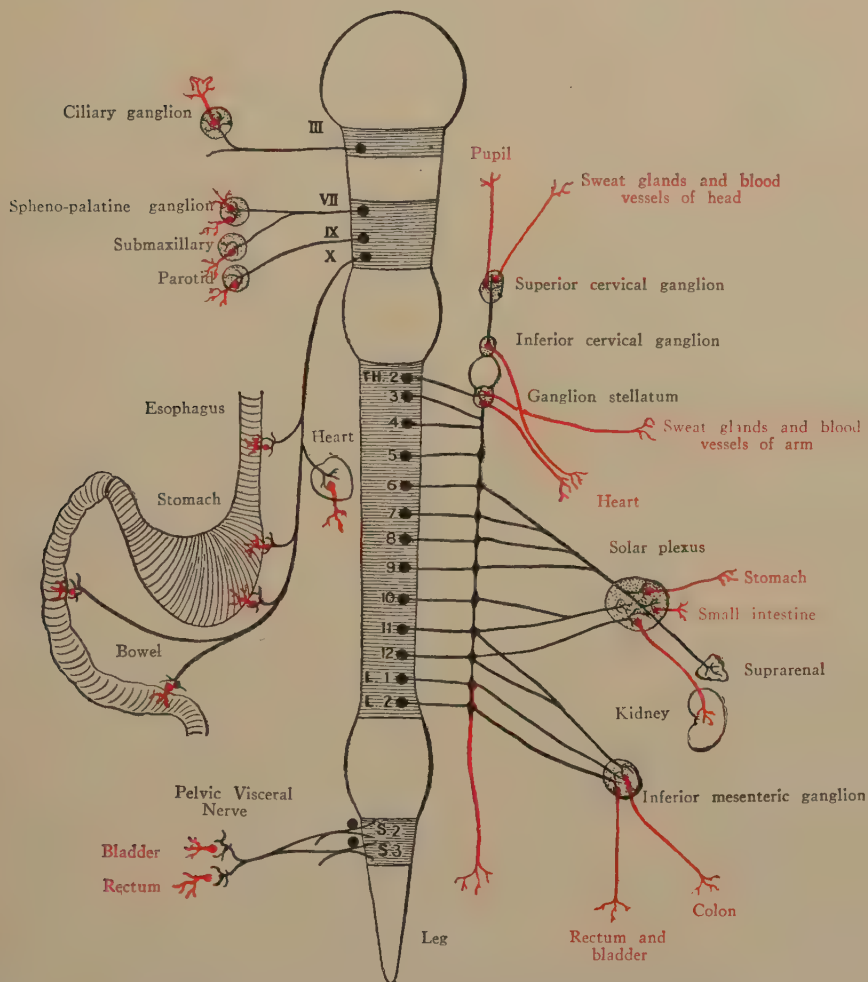


Plate I.

Scheme of the general arrangement of the Autonomic Nervous System, the distribution of the Sympathetic and Para-sympathetic portions being contrasted on the two sides of the diagram. Preganglionic (connector) fibers in black, post-ganglionic (excitor) fibers in red.

From Brown: The Sympathetic Nervous System in Disease.

tory neurosis, etc.—*with vagotonia or with sympathicotonia*; or, as is more frequent, with both states of hypertonia at once. It is not always possible in the clinic to make the distinction between hypertonia of the vagus and that of the sympathetic, however clear the distinction appears to be when contrasted in Eppinger and Hess's classic outline.¹⁵

On the other hand, the vegetative symptomatology itself is, in certain aspects, poorly understood and therefore writers include in the hypervegetative forms, symptoms whose true significance is more than doubtful. For example in the masterly description given by Eppinger and Hess of "vagotonic predisposition," of "vagotonia" and of "sympathicotonia" we find manifestations and complaints whose separate value is nil—arterial hypertension, extrasystoles, eructations, aerophagy and hyperchlorhydria for vagotonia; hypotension, slow digestion, dryness of the skin, easy febrile reactions, etc., for sympathicotonia. However, the entire syndrome suggested by the Viennese writers is clinically sensible and is sufficiently definite for diagnostic opinion, although I repeat, it is almost always merely a "basic syndrome," seldom an autochthonous one.

Vegetative Symptoms and the Climacteric

Of all the disturbances presented in association with vegetative syndromes the most frequent are the endocrine. Physiologically such is the functional correlation which links the glands of internal secretion with the vegetative nerves, that clinically there is no endocrine syndrome in whose symptomatology numerous manifestations of sympathetic or parasympathetic disturbances are not found. This occurs in acromegaly, myxedema, Addison's disease, diabetes, etc., *but above all in ovarian insufficiency and in hyperthyroidism*. Now, *ovarian insufficiency is the fundamental phenomenon of the menopause, and hyperthyroidism, as we have seen, is one of the most constant*. Thus, then, *the menopause is a state which will be particularly rich in vegetative symptomatology*.

¹⁵Eppinger and Hess: *Die Vagotonie*. Wien, 1910. This book is an example of the utility that certain hypotheses have in science, although in the long run they are not exact. The scheme advanced by Eppinger and Hess already is inadmissible, but few truths have been more fruitful.

Moreover, clinical observation confirms this. When we read concerning the "vegetative symptoms" as enumerated in any description we see that they are climacteric symptoms exactly, such as the changes of vascular tone (vasoconstriction and vasodilatation), palpitations, acrocyanosis, dermographism, disturbances of the sweat glands, angioneurotic edema, bronchial asthma, melanoderma, and angina pectoris. In short, all vegetative symptomatology is the same symptomatology which we find in the clinical forms of the critical age.

Thus, as has been said before, in the concrete case of the menopause—speaking in general terms—it follows that *vegetative symptomatology seldom appears alone*, but it is in just these patients that the syndrome of excitation of the vegetative nervous system attains, perhaps, a greater force. Indeed, we often see climacteric women whose sole symptomatology is limited to suffocations with heat flashes, spasms of the digestive tract, asthmatic attacks, angioneurotic edemas—phenomena, in short, dependent on the sympathetic and parasympathetic hypertonia. But in a much greater number of cases this symptomatology is obscured by the concomitance of other organic syndromes—such as circulatory, respiratory and endocrine.

Pseudohyperthyroid Vegetative Neurosis of the Climacteric

Here reference is made especially to a group of cases, important because of their frequency, wherein the vegetative symptomatology appears so balanced with the hyperthyroid that it is difficult to decide whether the case is one of hyperthyroidism with severe vegetative manifestations or a simple vegetative neurosis with hyperthyroid reaction. For just this reason I have given¹⁶ to these cases the provisional name "pseudohyperthyroid vegetative neurosis," understanding thereby the complex group made up of neuropathic, neurasthenic or hysteric individuals, with manifestations of the vegetative order, principally tachycardia, palpitations, subjective cardiac sensations, anxiety, tremors, violent vasomotor reactions, and even at times, loss of weight and slight increase in the size of the thyroid gland. These

¹⁶Marañón and Carrasco: Le métabolisme basal en clinique. Ann. de Méd. Paris, 1923.

cases are very numerous, and have been given diagnostic distinction by writers, and in medical thought, as *neurasthenia*, *circulatory neuroses*, *neocardiac asthma*, *irritable heart*, *vagotonia*, *vegetative neuroses*, etc. Of late years they have frequently been included under hyperthyroidism. By the clinical facts alone it cannot be denied that a certain degree of hyperfunction of the thyroid takes part in the production of the symptomatology. The determination of the basal metabolism is not likely to remove the doubt, since it almost always gives us in such cases, figures of questionable significance—between +15 and +25—which may as easily be interpreted as revealing a slight hyperthyroidism as a simple state of marked nervous irritability.¹⁷ Now these “pseudohyperthyroid vegetative neuroses” occur very often in women whose age rounds toward the sexual declination, or even in definitely menopausal women.

Therapeutic Conclusion

From the therapeutic point of view, this frequency with which the vegetative nervous system is hypertonic in the climacteric period has a confirmation in *the admirable result which, in general, is obtained by drugs which are sedative to the vegetative nervous system, particularly belladonna*, the use of which I constantly recommend in my clinic.

¹⁷I have recently demonstrated that in these cases the injection of a small quantity of adrenalin elevates the basal metabolism in proportion as the hyperthyroid factor is more marked in the genesis of the clinical picture. In this way we may bring out really latent states of hyperthyroidism as in another way serologic reactions may be evoked in masked syphilis. We assisted in the investigation of the findings of Tompkins, Sturgis and Wearn. A résumé of these studies appears in a monograph written by my student Micó: *Aplicación de la Accion de la Adrenalina sobre el Metabolismo Basal al diagnostico de los hipertiroidismos latentes*. Archivos españoles de Endocrinología y Nutrición, 1927.

CHAPTER VII

NORMAL MENOPAUSE AND PATHOLOGIC MENOPAUSE OUTLINE OF CLIMACTERIC SYMPTOMATOLOGY

Normal Climacteric and Pathologic Climacteric

Writers commonly speak of "normal menopause" and "pathologic menopause." In reality it is very difficult to determine the line which separates the normal from the abnormal in this crisis. Ideally, the climacteric should develop without any symptoms. The gradual extinction of ovarian function, compensated by glandular and nervous reactions, which I have described, should be accomplished so mildly that neither the woman herself, nor the observer could notice the change other than by the cessation of menstruation. But virtually this is exceptional. The crisis of puberty, however, does come on without the slightest subjective or objective disturbance when it occurs in organisms which are robust, and still free from the inevitable rust which later collects in the human machine. But the menopausal crisis comes after maturity, that is, at the apogee of sexual activity and in the fulness of social life. Consequently whether it be in woman or in man and however normal the life has been, the individual always reaches the critical moment with the body and the spirit weakened, disordered or diseased. And in particular the neuroglandular system, subjected as it is to the influence of emotional states—particularly in urban residents—has lost, practically always, the functional adaptability which would have permitted it to react to the involutional extinction of the genital function without pathologic fluctuations. Later we shall study the importance of these emotional states, whether slow or sudden. Of all the emotions there are two from whose profoundly disturbing action almost no one escapes in modern life. These are the *direct sexual emotions* and that emotion characteristic of our age—an emotion developed by the necessity of improving one's time

even anxiously—which we may call the *emotion of hurry*. Even this is sexual if rather indirectly, or *parasexual*, as I shall amplify later.

Temperaments and constitutional states which are then exaggerated, previous diseases of the various organs and apparatus, pathologic disturbances or simple physiologic abuses of the genital life, more or less intense emotional attacks—practically no one escapes from the influence of these trials. These, therefore, make a normal development of the climacteric impossible. There may be only simple “complaints” which are endured by women, enured to pain, almost silently, or at least without seeking medical aid. Others develop definite pathologic states which disturb life profoundly and may endanger it. And between these two extremes, the normal and the abnormal, lie all climacteric pathology. These two phases are so indefinitely expressed that we are forced to determine a priori what their limits are. In reality these limits are empiric and depend in large part on each individual’s subjective reaction to small deviations from the normal.

Thus then we shall limit our comment to description of each symptom complained of by women passing through the involutional period. We shall not attempt to designate the point at which the physiologic phase ends and the frankly abnormal begins.

Outline of Climacteric Symptomatology

Climacteric disturbances are of two kinds: (1) *chronologic*, that is, referable to variations in the date of the appearance of the menopause, aside from possible accompanying complaints, and (2) properly *clinical* upsets. These last may be divided in their turn, into three groups.

(a) Upsets or diseases which do not depend directly on the menopause but which elect this age for their development; such are, for example, certain uterine or mammary tumefactions and diabetes.

(b) Aggravations which the climacteric change causes in previously existing diseases; for example, breaks in the circulatory equilibrium in patients suffering with cardiac lesions previously compensated, or recrudescence of hepatic colics in lithiasic women.

(c) Symptoms directly dependent on the menopause, like palpitations, heat flashes, and obesity.

These last symptoms, the truly menopausal ones are endocrino-vegetative. They are the expression of the different glandular and nervous upsets described in the previous pages. In the majority of cases, as we have seen, these adopt a certain type, a combination of ovarian insufficiency and a hyperfunctional reaction of the thyroid and of the suprarenal system, with consequent hypertonia of the vegetative nervous system.

In the following chapters we shall study these chronologic and clinical changes. But first let us consider the general etiology of these climacteric symptoms.

CHAPTER VIII

GENERAL ETIOLOGY OF CLIMACTERIC SYMPTOMS

Constitution, Temperament and Internal Secretions

The *constitutional state* and the *temperament* influence climacteric symptomatology in a decisive way. This is natural. We cannot go into the problem here as to the respective limits of the two concepts, *constitution* and *temperament*. This has been amply discussed in the literature and each time more bitterly. Indeed, reading most of the recent contributions on this point does little or nothing to clarify the perplexity of the uninitiated. Such perplexity may even be increased by the new distinctions made and the terminologies of doubtful utility. By constitution we mean that complex of somatic, nervous and biochemic characters which, unmodifiable in their fundamentals, are transmitted through heredity. These are the groundwork, while temperamental states are like diathetic states. The *temperament* is a peculiar mode of reaction on the part of the neurohumoral system of each individual. This reaction is due partly to the constitution and is also influenced by external causes, such as the physiologic medium and diseases. The constitution, then, is rather static or permanent. The temperament is rather dynamic, functional and susceptible to modification. We might say, forcing the figure, that *the temperament is to the constitution as the function is to the organ*.

It is now known that there is a close relationship between these old concepts, constitution and temperament, and the endocrine glands. This fact is the sole unquestioned bit of knowledge advanced by modern experimental medicine. The endocrine glands, always collaborating with the vegetative nervous system, act primarily upon the somatic cast, inherited by the individual, on one side—that is to say, upon his constitution; and on the other side the glands influence the mode of this reaction in the face of normal and pathologic stimuli. That is, the endocrine glands act upon the temperament. Most of the authoritative writers of

late years—like Bauer,¹ Viola,² Pende,^{3, 4} and Biedl⁵—recognize this. Berman⁶ has devoted a book to this question alone. And above all others we must mention Kretschmer's work,⁷ not only as the contribution of a neurologist, rather than an endocrinologist, but because of his success in harmonizing the many discordant theories. Looking at the subject from the modern point of view, Kretschmer emphasizes the perfect correlation existing between the corporal and the psychic parts of the individual—or between his constitution and his temperament—because both depend upon a single cause. That is, both depend on the functional vigor of the various glands of internal secretion, on the "endocrine formula" peculiar to each individual. This expression, indeed, is one which I⁸ suggested many years before Kretschmer, and in the same sense.

It would be unfitting here to attempt to reconstruct the classic constitutional and the classic temperamental states on the basis of their corresponding endocrine formulas. But by way of example let us consider the difference between the inhabitants of the North and of the South of Spain. Those of the North are a vigorous, athletic type. They are frequently fair, blue-eyed, and even-tempered. Dentition is deficient. On the contrary, the inhabitants of the South of Spain are thin and swarthy. Their eyes are dark, their teeth magnificent. These people are restless and superficial. Nothing can better explain the contrast between these two groups than their different thyroid constitutions. The North—the region of the Pyrenees—is a district where thyroids are poor in iodine, where there is a tendency to goiter with hypothyroidism. The South—the Mediterranean coast—is a district where thyroids are rich in iodine, constitutions are hyperthyroid and there are frequent cases of pathologic hyperthyroidism. A large part of our enormous number of hyperthyroids come from the

¹Bauer: *Die konstitutionelle Disposition zu inneren Krankheiten*, Berlin, Springer, 1920.

²Viola: See a résumé of his work in *La Costituzione nel suo moderno significato. Endocrinologia é Patologia Costituzionale*, Rome, 1922, i, 9-16.

³Pende: *Op. cit.*, note (17), page 19 and also in the admirable treatise by the same writer.

⁴Pende: *Dalla Medicina alla Sociologia*, Palermo, 1921.

⁵Biedl: *Op. cit.*, note (15), page 19.

⁶Berman: *Op. cit.*, note (32), page 21.

⁷Kretschmer: *Körperbau und Charakter*, ed. 3, Berlin, 1922. Kretschmer has published a popularized résumé of his point of view in *La Revista de Occidente*, Madrid, No. II, 1923; in this, the German title is aptly translated by the expressive Spanish phrase *Face and Character*.

⁸Marañón: *Op. cit.*, note (1), page 18.

south of the peninsula. Pende⁹ has made the same observation in Italy. In countries where the hypothyroid tendency is even greater than in our Pyreneal provinces, the tendency toward an athletic constitution and a prudent and parsimonious temperament is also more marked. Not long since DeQuervain, of Bern, told me that the traditional cachexia of the Swiss is, in reality, nothing more than an attenuated and racial form of hypothyroidism. [The situation in North America is somewhat similar to that outlined by the author for Spain. On this continent we have the well-known "goiter belts," or areas of thyroid deficiency. These are chiefly the region in the northwest about Seattle, the Great Lakes region extending into Canada, and the Pennsylvania region. In this country, however, the situation is modified by several conditions not pertinent to Spain. Here the population is represented by an influx of various races, chiefly from northern and southern Europe, implanted upon the original American stock. Further there has been a constant current of travel, giving to the population a sort of fluidity, the direction being generally from east to west. These two sociological factors alone must inevitably modify completely the situation with respect to hyper- and hypothyroid tendencies.—C. C.]

What I have said of hypo- and hyperthyroidism can be said of the other glands. Pende¹⁰ gives a series of alternate temperaments, such as hypergenital and hypogenital, hyper- and hypopituitary, hyper- and hyposuprarenal, besides hyperthyroid, hypothyroid and dysthyroid temperaments. Thus Pittaluga¹¹ may properly say that "endocrinology is, in reality, the pathology of the temperament."

Influence of Temperament on Climacteric Symptomatology

The influence of the temperament upon climacteric symptomatology is now well understood. We have seen that during the critical involutional period the other glands react anatomically and functionally thus compensating the insufficiency of the failing ovary. *It is evident that this reaction will be determined to*

⁹Pende: Op. cit., note (4), page 82.

¹⁰Pende: Op. cit., note (17), page 19.

¹¹Pittaluga: Discurso de contestación al de resección en la Real Academia de Medicina de G. Marañón, Madrid, 1922.

a certain extent by the previous functional state. That is, the reaction is determined by the temperament. Hence, in women of "asthenic constitution" and *hyperthyroid temperament* the hyperthyroid reaction of the menopause will be presented much more frequently and more intensely than in women of "lymphatic constitution" and *hypothyroid temperament*. Parallel to what I said of the distinct geographic distribution, in the Spanish peninsula, of the cases of pathologic hyperthyroidism and hypothyroidism, I may now add that the hyperthyroid form of the menopause—almost constant in the South—is less frequent in the North. Statistics which we have compiled prove this, and certain practitioners, like Dr. Martinez of Santander, bear us out. These women with *hypothyroid temperaments* find their symptoms accentuated on reaching the involutional crisis. Some are even converted into true cases of myxedema.

If a woman exhibits the signs of a *hypersuprarenal temperament*, in the menopausal crisis those phenomena which we have given as probably dependent on hypersuprarenalism will predominate. This *temperament* is, like the hyperthyroid, very frequent and corresponds to Frank's¹² *hypertonic temperament*. Its characteristic signs are the following: corpulent, massive morphology, tendency to ectopic hairiness—as on the upper lip, chin region and on the arms and legs—voice of contralto type, energetic character, virile mentality, free, bold movements like a man's, tendency to hypertension and to glycosuria. These women, perhaps without losing any of the charms of their sex, stand morphologically at the end of the scale where the opposite sex begins. These women who are energetic, who are able to bear responsibility and difficult situations easily, suffer more profoundly than others the virile transformation in morphology and spirit on reaching the menopause—a transformation scarcely noticeable in very "womanly" women, those who are delicate, fragile, childish—that is, endowed with a weak suprarenal system.

In women with a previous *hypopituitary temperament*, that is to say with a hypophysis inclined to hypofunction, with a tendency to obesity and weak sexual functions, the menopause will

¹²Frank: Bestehen Beziehungen zwischen chromaffinem System und der chronischen Hypertonie des Menschen? Deutsch. Arch. f. klin. Med., 1911, ciii.

come early. Furthermore, it will be characterized by a predominance of localized deposition of fat, principally on the abdomen, hips and bust.

If the *hyperpituitary* signs predominate—such as tall stature, enlarged features, well-developed extremities, deep voice, hirsutism—the menopause will accentuate them, initiating a sort of acromegaly. (See page 72.) We might add other examples of temperaments but they are less frequent than those which we have just considered.

It is obvious that there are a great many women, the best nourished group, who have no definite temperament and to whom, therefore, the above remarks are not applicable. When attempting to apply any classification of constitutional or temperamental types to a large number of individuals, one fact, which is usually forgotten, must be borne in mind. This is that the temperament, be it what it may, represents a type of selection, the first step toward a disposition and in consequence will be observed in only a limited number of individuals. But the immense majority of people presume to tell us that they “have no temperament.” Then we can only say that the menopause will, in these cases, be developed under the exclusive influence of the momentous causes we shall comment upon soon.

Previous Pathologic States and Climacteric

It is a fact of common observation that pathologic states which have been latent or have presented only a mild symptomatology, on reaching the involutional crisis begin to manifest themselves or to be accentuated. Clinical experience confirms this as we shall see in the chapter devoted to climacteric pathology. *Nervous and circulatory upsets are especially influenced by the change of life and give rise to very peculiar symptoms in the clinical picture of the menopause.* During this, both systems—the nervous and the circulatory—are put to proof, and any change in their usual function becomes particularly noticeable.

In less degree this *revealing* influence also extends to the other systems and apparatus of the body and each one may put its stamp on the menopause.

Influence of Genital Disturbances

From the point of view of this predisposition it is natural that the previous disturbances in sexual activity should have a special value. Here we must consider three classes of facts.

1. The existence of lesions in the genital organs, which nevertheless affect function, such as tumors or displacements of the uterus, or chronic inflammatory involvement of the genital tract. These give rise to certain symptoms in the menopause, particularly hemorrhagic, circulatory and nervous disturbances.

2. The way in which the woman exercised her sexual activity. This factor reacts directly on the endocrine activities of the ovary. The crisis will not be the same in a woman who has borne children as in one who was sterile. It will not be the same in one who has conceived a discreet number of times as in another who has been weakened by an excessive number of pregnancies; nor the same in one who made an unnatural use of her sexual activity as in one who exercised it in the tranquil atmosphere of her own home. Still less similar will it be in the woman who reaches the menopause in a state of chastity. And within this last group it will differ in her who remained celibate without emotional struggle (because of the frigidity of her temperament or through the voluntary abstinence of a religious devotee) from the crisis in another who remained so by necessity because of the social conditions which keep so many women of perfect sexual aptitude in an enforced spinsterhood.

3. The previous endocrine potency of the ovary is another factor. The woman who possesses a hypoplastic ovary, a certain grade of sexual infantilism, will see her specific activity disappear more quickly and with less disturbance than one with very active ovaries, ardently sexual, who retains her function until very late and is parted from it with profound disturbances of her whole organism.

All these conditions—properly *genital*—act especially on menopausal chronology and I shall speak of each one in turn later.

Emotion and Climacteric

The influence of *emotion* must receive more detailed comment and requires a separate chapter.

CHAPTER IX

EMOTION AND THE CRITICAL AGE

Outline

In climacteric pathology emotion plays a particularly intense and definite rôle. My experience has given me firm convictions on this point, and the subject should be dealt with at some length, not only because of its clinical phase but also because of its relation to certain involved physiologic reactions. These are under much discussion at present.

My point of view is this: *the endocrine-vegetative system undoubtedly takes part in the development of the emotional act although the kind of intervention is controversial. It is certain at least that the greater or less emotional predisposition depends in large part upon the endocrine-vegetative factor and that the undeniable pathologic repercussions which emotional states exercise on the organism take place through the medium of this same endocrine-vegetative system. In the critical age the endocrine-vegetative system usually acquires a degree of functional tension which makes it particularly fit for emotional receptivity. As this physiologic condition coincides with a parallel social condition—that is, with the increase of emotional attacks—the organism is frequently profoundly affected through psychic impulses. In the following chapters we shall study the syndromes which are thus produced, and I shall endeavor to support my proposition with facts. This is a matter concerning which I have written for several years, progressively modifying my first interpretations as new observations appeared. But my convictions have been repeatedly confirmed along the fundamental lines, just set down.*¹

¹: cf.

(a) Marañón: Sobre el mecanismo de la emoción, Ateneo de Madrid, December, 1920.

(b) Marañón: La reacción emotiva de la adrenalina, Medicina, Ibero, 1920.

(c) Marañón: Breve ensayo sobre la edad y la emoción, Conferencia en la Universidad de Salamanca, March, 1921. (Published in Archivos de Medicina y Cirugía, Madrid, 1921.

(d) Marañón: Introducción al estudio de la teoría neurohumoral de la emoción Conferencia en la Universidad de Valencia, May, 1921, Published in Policlínica, Valencia, 1921.

I shall take up the points in question in the following order.

1. Intervention of the endocrine-vegetative factor in the emotional act. Emotional predisposition and internal secretions. Endocrine-vegetative mechanism of the pathologic disturbances of emotional origin.

2. State of the endocrine-vegetative system in the climacteric age. The critical age is the one of greatest emotional instability.

3. Increase of emotional attacks in the climacteric.

4. Clinical facts: coincidence of the climacteric and grave emotional attacks in the etiology of symptoms proper to this age.

Physiologic Analysis of Emotion

The only way to make any progress in considering the emotional moment is along physiologic lines, since, with isolated exceptions, psychologists have made little progress in its study and have now exhausted the possibilities of investigation from that angle.

We may break up each emotion into three elements: a psychologic element, an expressional element, and a vegetative element. The *psychic element* is the cerebral concept of the idea, the remembrance or the sensorial impression which gives rise in each case to mirth, sorrow, anger, etc. The *expressive element* is a complex of movements of the locomotor apparatus (attitudes) and of the muscles of facial expression (grimaces, accompanied at times by articulate or inarticulate sounds) by means of which the emotional state is manifested externally. The third element, which I have called *vegetative*, consists of a series of visceral changes which the individual experiences and perceives and thanks to which he possesses emotion.

Psychologists formerly concerned themselves only with the first element, the *psychic*, and they still prefer to do so, in spite of the

(e) Marañón Contribution a l'étude de l'action emotive de l'adrenaline. Rev. franc. d'Endocrinologie, 1924.

Patología e higiene de la Emoción, Siglo Médico, 1924.

As this is not the appropriate place, I refrain from discussing comments, favorable and unfavorable, evoked by my articles on emotion. cf.

(f) Turró: La Emoción, Siglo Médico, 1919.

(g) Sierra: Estudio psico-pathológico referente a la emoción experimental, Semena Médica, Buenos Aires, 1921.

(h) Mut: Algo acerca de la frenocardia y otro poco sobre la emoción, de Marañón. Revista Iberoamericana de Ciencias Médicas, July, 1922.

(i) Mira: La bipolaridad emocional, Psiquiatría, 1922.

(j) Rosés Lacoigne: Psicología descriptiva. Buenos Aires, 1923.

reiterated insistence with which some of them, particularly James,² call attention to the importance of the visceral changes. Indeed, Aristotle, in defining "the passions," spoke of a "bodily change," which, as we shall soon see, was the basis of passion. Yet this observation passed unnoticed by the physiologists and psychologists who followed him even up to the modern era. The study of the second element, the *expressional*, fell first to artists, and then to the pseudoscientific who studied the expressions of the human physiognomy as a means of deducing the psychic status of the individual. Finally knowledge of this expressional element reached a completely scientific era which culminated with Darwin.³ To his studies, in that they were actual observations, it has been possible to add scarcely more than relatively secondary details.

Exact knowledge of the third, or *vegetative*, element is of recent date. It was first developed, as we have said, by William James, the psychologist, and also at almost the same time by the Danish physiologist, Lange.⁴ Progress along this line was held back in spite of the efforts of Sergi, of Serrington⁵ and various others, although these were not numerous, until the present time when knowledge of the endocrines threw light on the problem, thanks principally to Cannon⁶ and to several other writers.

This *vegetative element* is—and this appears to me to be a fundamental idea—*common to all the emotions*, within certain limits. Each emotion, indeed, is differentiated clearly from the rest by its psychologic content, the mental concept in anger being perfectly distinct from that in tenderness, or in grief, or in joy. This distinction also exists in the expressive element, but here not with the same clarity, especially in proportion as the phenomena of expression leave the locomotor system and approach the vegetative system. Thus, for example, intense joy is expressed, particularly in children, by a peculiar motor exultation,

²James, W.: *The Principles of Psychology*, New York, 1890.

³Darwin: *L'expression des émotions chez l'homme et les animaux*. French edition—Pozzi et Benoit, Paris, 1890.

⁴Lange: *Les émotions*. Dumas' French edition, Paris, 1911.

⁵Serrington: Experiment on the value of vascular and visceral factors for the genesis of emotion. *Proc. Roy. Soc. London*, 1920, v, 66.

⁶Cannon: *Bodily Changes in Pain, Fear and Rage*. New York, 1915. However, in several modern works on psychology allusion is made to these physiologic and endocrine viewpoints. I shall mention the admirable manual by Thouless, *Social Psychology*, London, 1925.

leaping, clapping the hands, and the like. Profound sorrow is expressed by muscular depression, by an immobility of the limbs and a general wrinkling of the face. The distinction from the motor point of view is then evident. On the other hand, tears, which are an expressive phenomenon of typically vegetative nature, gush forth in moments of intense happiness as well as in those of great grief.

And this indistinctness is accentuated when we come to the third element of emotion, the vegetative, expressed by the visceral vibration, which in its component elements is common to every class of emotional states. The disturbances in cardiac rhythm, the vasomotor changes, the changes in arterial pressure, the changes in the eyeballs and so forth do not have, at least by themselves, any specific value, since they may be presented in the most opposite states of mind, with infinite variations in their intensity and in the way they are combined. The common people well express this lack of specificity of the vegetative elements of emotion in a multitude of phrases in current use. One speaks, for example, of "being white with rage," "white with anger" and "white with fear"; "quivering with enthusiasm," "with anger," and "with fear"; "weeping with joy," "with rage," and "with sorrow"; "trembling with anxiety," "with fear" and "with joy," and so on. And the physiologic analysis of these vegetative changes in emotion, which we cannot give here, coincides exactly with such common expressions.

We may turn back now to call attention to the value of the common concept of emotion in spite of the opinion of psychologists. Psychologists speak of the emotional states as different entities, struggling to establish the characteristics and the limits of each one separately—such as joy, sorrow, and admiration; while the layman speaks of "emotion" as something generic and indefinite. The layman speaks of some one's being "moved" without differentiating the emotion into its proper class. Another he says, is "very emotional," meaning that he is sensitive to all emotion, not to any one in particular. In emotion, then, the layman perceives that which constitutes its physiologic root, the *visceral commotion*, Aristotle's "bodily change"; the internal tremor, the accelerated or the slowed heartbeats, the shivering

which runs over the skin, the oppression in the chest, the changes in the color of the face—all the phenomena, indeed, which we perceive when any intellectual sensation of any sort is sufficient to be converted into an emotion. These phenomena, as we said before, are always the same.

This complex of common vegetative phenomena constitutes, however, *the essential condition of emotion*. Thus each of us may have at any time, voluntarily or involuntarily, *thoughts of pain, happiness, love or revulsion, but without any emotion. And we can feign voluntarily almost all the phenomena expressive of the corresponding emotional states, but also without emotion*. This is the case with actors, barring moments of inspiration. For emotion to occur *it is necessary that the psychic concept and the complex of expressive phenomena should set up visceral vibration*—that is, the vegetative factor must enter.

Intervention of the Endocrine-Vegetative Factor in the Emotional Act

Now this vegetative or visceral element, the keystone of emotion, is closely related to endocrine-vegetative changes which I shall briefly analyze. All the vegetative phenomena of emotion which I have enumerated lie, indeed, within the sphere of the nervous vegetative system which is composed (as we saw in Chapter VI) of three parts, *cranial, sympathetic and sacral*. Excitation of the nerves of this system gives rise to all the disturbances which characterize the organic moment of emotion, wherefore, until recently, the emotional phenomena was considered the product, pure and simple, of a discharge of this vegetative nervous system. But now we know that the vegetative nervous system functions in intimate and inseparable connection with all the glands of internal secretion in such a way that the vegetative nervous influence affects the functioning of the glands of internal secretion, and in turn, the secretion of these glands affects the functioning of the nervous system.

The function of the vegetative nervous system and that of the endocrine system being so close, so impossible to separate, it is readily understood how the latter will also intervene predominantly in the mechanism of the emotional act. Experimentation

and clinical observation confirm this supposition so that at present the collaboration of the humoral factor in the emotional act is generally accepted in biology. Of many proofs, all of which I cannot enumerate here, I shall cite the following case which I described some years ago⁷ and which I have again carefully gone over in a later report⁸ "*the emotional reaction of adrenalin.*" It is as follows:

Emotional Reaction of Adrenalin

If, in a *predisposed subject*, we inject subcutaneously a small quantity of adrenalin (the most important internal secretion of the suprarenal glands), we can observe in him a complex of visceral changes which exactly reproduces those causing a violent emotion in the individual. Within a few moments after injection the pulse becomes rapid, the heart beats violently, the face pales. A sensation of more or less intense thoracic oppression forces the subject to breathe deeply; the mouth is dry; the hands, and sometimes the entire body, are seized with a tremor either fine or coarse; and lastly "goose-flesh" may appear around the site of the injection and at times extend rather far beyond it.

It is obvious that these adrenalin phenomena, as just described, are identical with those which accompany any emotional state of moderate intensity. In certain individuals this similarity is so great that the subject himself identifies the upsets which are occasioned by the drug as such emotional phenomena and spontaneously declares that he feels "the same as when I am afraid," but adds that he is "calm."

Frequently the one subjected to such experimentation remarks the resemblance between his state and that experienced in moments of anguish. But such a patient always adds that there is a difference inasmuch as he now retains psychologic calm. I have repeated these experiments innumerable times, taking pains to avoid all possible causes of error. The results have been confirmed by other writers, among them Cawadias⁹

⁷Marañón: Op. cit., note (1b), page 87.

⁸Marañón: Op. cit., note (1e), page 88.

⁹Cawadias: La fièvre d'origine sympathique. Ann. de Med., 1921.

and Sierra.¹⁰ For example, Cawadias states that one of his patients, on perceiving the effects of the injection of adrenalin, exclaimed, "I feel as I did the day they imprisoned me, but I am calm." This was a woman who had been detained and shut up in a fortress a few months before. I have collected analogous expressions which I have heard at various times in my experiments.¹¹

That is to say, by introducing into the system a small quantity of this chemical substance which our organism itself elaborates and injects (if I may use the word) into our blood, we can reproduce at will the emotional organic commotion, the "bodily change," independently of what passes in the cerebrum. We can then, *at will, separate organic emotion from psychic emotion*. And it is unnecessary to emphasize the importance which this fact has in establishing the problem of emotion on an experimental basis.

Other similar cases are extremely interesting. There are some in which the organic agitation caused by adrenalin is so violent that the subject *not only gives an account of its identity with the emotional commotion, but his brain, on receiving this sensation, associates it with an affecting recollection, generally sad, and then the emotion is completed and suddenly cries of anguish occur with abundant tears and sobs*. And in another group of individuals, if the psychic emotion does not occur spontaneously, it is suggested sufficiently, so that the subject gives way to it easily and sometimes impulsively. [I have repeatedly observed reactions of the nature here described during the experimental work incident to the preparation of my paper on the menopause.—C. C.]

For example, taking the case of one woman from among my numerous observations. I inquired into her emotional past and she spoke calmly of her absent children; of her parents, dead some time; of her husband, who worked in another country. She was a woman of the people, inured by adversity and re-

¹⁰Sierra: Op. cit., note (1g), page 88.

¹¹Here are some phrases I have found in texts, in the course of investigation: "I feel as if I were afraid": "as if I anticipated some great joy"; "like an internal surprise," "as if I were deeply moved"; "as if I were going to cry without knowing why"; "as if I were in great fright, but I am calm," etc.

signed to everything. She had come to the hospital to be operated upon for a gynecologic infection. I injected three-fourths of a milligram of adrenalin and in seven or eight minutes her body underwent the changes described above. She became pale, trembled slightly, felt that her heart beat violently, that her chest was oppressed—but she was calm and smiled on recounting these sensations. Suddenly I began asking again about her children, and instantly, as if the memory (inactive a moment before) were the trigger of a loaded weapon she broke down, weeping copiously, ceaselessly repeating the names of her absent loved ones.

Emotional Predisposition and the Endocrine Vegetative System

We have noted that this emotional reaction does not present itself in all subjects, *but only in those who are endowed with a predisposition, with a sufficient emotionalism*, and it is most interesting to add now that these predisposed individuals are *almost always those who present more or less clearly symptoms of hyperthyroidism*. Patients affected with Basedow's disease are those who suffer the emotional reaction of adrenalin more. In these the thyroid hyperfunction reaches its maximum degree. On the other hand, in the myxedematous, patients in whom the thyroid function is extraordinarily diminished or nearly exhausted, the reaction is apt to be negative. And in normal subjects who are ordinarily but little sensitive to the reaction, *sensibility may be increased by treating them beforehand for some time with thyroid extract* in doses sufficient to provoke those symptoms called therapeutic hyperthyroidism. In this situation the adrenalin acts *immediately* on this sensitized field, the appearance of the vegetative phenomena which characterize the emotion depending directly on it. The results of other writers, particularly Cannon,¹² confirm this *releasing* rôle of adrenalin in organic emotion. All hold to the belief that for an affective concept to be formed in the brain there must be a nervous impulse transmitted across the splanchnic nerves up to the suprarenal glands, provoking in them a sudden secretion of adrenalin which gushes out into the blood stream and gives rise

¹²Cannon: Op. cit., note (6), page 89.

to the greater part of and to the most characteristic phenomena of the vegetative emotional commotion.¹³

Some writers, like Achucarro,¹⁴ and Turro,¹⁵ hold to the hypothesis that in this moment of passage between the cerebral instant and the vegetative the *neuroglia* intervene. These are endowed, according to some writers, especially Nageotte, with an internal secretion which links the function of the nerve cell directly to the blood wherein the neurologic branches are supported. This hypothesis has broken down. However, the admirable histologic part on which its author based it remains.

Independently of the *pure emotional potentiality* of the sensation, of the idea or of the memory origin of emotion, the first thing that can be said against the explanation given above is that the individual will suffer the affecting shock more or less as his endocrine vegetative system has more or less reactional capacity. Clinically we can determine the functional state of this system principally by an examination of the suprarenals and particularly of the thyroid. Or, in other words, the *emotional index* of each individual is in direct relation to the *functional index of his endocrine-vegetative system*, and practically of his thyroid function. This hypothesis is well proved clinically, since subjects with hyperthyroidism are exquisitely sensitive to all the emotions; while the hypothyroid, the myxedematous, have a blunted and indifferent emotional sensibility. The patients with insufficient suprarenal, those with Addison's disease, are in turn characteristically apathetic. The other extreme is wanting, since the hypersuprarenal syndrome, if it exists, is yet to be clearly defined. The symptoms of the so-called *emotional constitution*, described chiefly by Dupre,¹⁶ coincide almost point for point with the symptoms of a hyperthyroid temperament. The principal signs of the latter are, thinness, motor restlessness, a lively and shifting glance, dark and abun-

¹³As I do not intend to give here a complete bibliographic study of the modern points of view on emotion, I make no reference to various writers whose arguments are similar to mine. Nevertheless I may mention Buscaino's book, *Biologie de la vite emotive*, Bologne, 1921, upon which I shall comment later at length.

¹⁴Achucarro: *Nuevas alteraciones en el sistema nervioso de animales hipertiroidizados*. Bol. de la Soc. Esp. de Biol., 1916.

¹⁵Turro: *Op. cit.*, note (1f), page 88.

¹⁶Dupre et Grimberty: *La psychonevrèse émotive*. Rev. Neurol., 1917, p. 45.

dant hair, unstable circulation, sweating easily provoked, liveliness of the motor reactions, exalted psychology, that is to say, the same characteristics which the layman assigns to persons who are passionate, irritable, and sensitive to the states of emotion. They are the somatic characteristics of Don Quixote de la Mancha, whose sublime emotional facility harmonizes so well, so inevitably, with his somatic signs. "That tall, withered body, with its thin face, long, brown limbs, grayish hair, curved and aquiline nose and large drooping mustaches" is, according to Sampson Carrasco, a description of a hyperthyroid. Unamuno¹⁷ also points out that the temperament of the immortal Knight is that which Huarte called "hot and dry," which is precisely the same temperament which we now call hyperthyroid.

This participation of the endocrine-vegetative system in the emotional act helps to explain many cases of pathologic states consequent to emotion, either intense and sudden, or prolonged and depressing. Therefore, a great part of the nervous syndromes described as consequence of emotional states, a large number of emotional neuroses, are vegetative neuroses, with evident endocrine symptomatology. Sometimes this is confused, as in those states which I¹⁸ have called "pseudohyperthyroid vegetative neuroses." These are cases where the writer in reporting them has used qualifying terms, such as vasomotor neuroses and cardiac neuroses, gastrocirculatory neurasthenia, or hysterism, but which always present a certain number of symptoms analogous to those of hyperthyroidism, tachycardia, palpitations, loss of weight, and tremor of the hands. Their relation to true hyperthyroidism is much discussed just at present since the problem has not been solved by any of the proved functions of the thyroid nor even determination of the basal metabolism.¹⁹ Other times the consequence of the emotional shock is a typical hyperthyroidism, a subject upon which the European war has furnished an abundant bibliography. This I have summarized, contributing at the same time considerable favorable experience of my own.²⁰ Cases of youthful ovarian insufficiency

¹⁷Unamuno: *Vida de Don Quijote y Sancho*, Madrid, 1914.

¹⁸Marañón et Carrasco: *Op. cit.*, note (16), page 76, and *Societe de Biologie de Paris*, June, 1924.

¹⁹*Cf.* note (17), page 77.

²⁰Marañón: *Hyperthiroidisme d'origine emotional*, *Ann. de Med.*, 1921.

are also very frequent, as are those of Addison's disease,²¹ of myxedema, acromegaly and so on, all clearly apparent after an intense emotional impression. It may be stated that in all these the emotional, endocrine-vegetative reaction, either through the violence of the emotional attack or through its persistence, instead of being transitory and physiologic, becomes pathologic and permanent, "crystallized" clinically into this or that syndrome according to the previous predisposition of the individual, perhaps also according to the intensity, the mode, or the persistency of the emotional shock.

In other pathologic states of a pathogeny very distinct from the endocrine-vegetative the participation of the latter system may be evoked. The emotional states may intervene in the course of these conditions although they take no part in their production. Such are, for example, cancer, infections, dyscrasias. These are all influenced unfavorably by emotion as is the common experience of every physician. The tone of the endocrine-vegetative system, that regulator of organic equilibrium, depends in part on the amount of resistance which the organism can muster in the face of pathologic attacks.

Organic (Endocrine-Vegetative) Predisposition to Emotion in the Critical Age

With the foregoing explanations in mind we can now comprehend the special vulnerability of those passing through the climacteric epoch in the face of emotional trials. Indeed, as I have previously stated, in this age the thyroid and suprarenal glands, which have the most influence on the endocrine-vegetative reaction in emotion, acquire their maximum functional tension. We have already seen that in a great many climacteric men and women there are found either indefinite syndromes or clear manifestations of hyperthyroidism. In regard to suprarenal hyperfunction, although more doubtful, it is also very probably the origin of some of the clinical manifestations of the climacteric.

²¹I cite, because it is the first case which appears in the literature on the Addisonian syndrome, a case reported by a nonmedical writer. Father Siguenza, 1690, reported the case of a priest in charge at the Escorial who developed this disease as a consequence of the terror which he felt at the fall of a thunderbolt at the monastery. Marañón: El primer caso conocido de enfermedad de Addison, *El Siglo Médico*, 1922).

This thyroid and suprarenal hypertonia and the consequent neurovegetative hypertonia *constitute, then, a permanent state of emotional predisposition.*

Elsewhere²² I have attempted to demonstrate that just as intellectual abilities go through a rather fixed cycle in the life of the individual, so the emotional ability goes through similar phases in different subjects in the different stages of organic evolution. And in this emotional curve the culminating point corresponds to the age of transition between maturity and senile descent, that is, the climacteric. Contrary to common opinion that the repetition of emotion dulls the sensibility, it is certain that the emotional aptitude widens considerably, sometimes suddenly, on passing the fortieth year, and that, too, independently of apparent insensibility due to "professional habit." Apart from this quantitative increase in susceptibility to emotion, and perhaps still more characteristic, there is observed a sensitization toward the whole range of emotions which in younger years affected the individual only in a secondary way. Such are those which James called "delicate emotions," the most intimate and disinterested which we may term "lyric emotions" as opposed to "epic emotions" proper to youth. Details of everyday life which previously passed unnoticed, musical and literary sensations, wonders of nature, in short, emotions of "small vibration," which for years have not provoked reaction in the human spirit, in the climacteric produce profound commotion. We shall see, presently, in speaking of the psychic symptoms, that this "emotional instability" is clinically characteristic of the critical age. If in this age the human spirit is presented to us in full maturity, it may be said that it is, above everything else, its emotional capacity which has reached its fullest development.

Increase of Emotional Attacks in the Critical Age

To produce this result there come, as I have said, from one side the greater predisposition of the neuroendocrine system and alongside this "endogenous" factor, the "exogenous" or

²²Marañón: Op. cit., note (1c), page 87.

social factor, *the evident increase of emotional attacks in this age.* "It appears," says Vinay,²³ "that the frequency of the misfortunes inseparable from life are greater in this epoch; in reality this is not so. These accidents are not more frequent than in other periods of life. What happens is that patients are less able to struggle against ill fortune. Their sensibility is heightened and their resistance diminished."

The French writer is correct only in the close of his statement. Sensibility is increased, indeed. But the frequency of emotion, generally of a depressive type, is really greater in this age. After maturity, with each year that passes the successes of the present diminish and illusion as to those of the future fades. Physical weakness begins. The family and created relationships multiply the reasons for the feeling of depression, and everything at last becomes tinged with the bitterness of old age. The crowding up of the next generation further accentuates this by contrast as one begins to see the loss of one's own youth. *Emotional attacks, then, besiege the spirit just when it is most vulnerable.* This obtains until old age is reached when the emotional mechanism is dulled. Hence the last years of existence are apt to be less turbulent, at times particularly happy.

Frequency of Emotional Etiology in the Pathology of the Climacteric

In harmony with the foregoing, clinical observation shows us that in the majority of pathologic symptoms of the climacteric, both in men and women, there are these emotional antecedents. An intense emotional state coincides, at times, with the beginning of some such cases. The emotion may be either sudden and exciting or, as in the greater number of cases, of a depressing nature. *Menopause and emotion are two inseparable factors.* The reasons which I have set down explain their coincidence, which is of fundamental importance in the study of climacteric psychology.

²³Vinay: Op. cit., note (12), page 19.

CHAPTER X

TIME LIMITS OF THE CRITICAL AGE AND CIRCUMSTANCES WHICH MODIFY THEM. EARLY MENOPAUSE AND LATE MENOPAUSE

Exact Time Limits of the Critical Age Impossible

The data referring to the menopause, that is, pertaining to its onset and duration, have been well appraised by gynecologists and will not detain us long. To the most generally accepted opinions I shall add some suggestive comments from my own experience in the light of my theory.

The figures, given by writers, for the *time of the onset of the menopause* are exceedingly variable. This is logical. It results from the childish attempt to locate, by force of statistics, in a set year a period of life which is itself extraordinarily complex and variable. I have already said that the cessation of the menstrual flow, which is the starting point for gynecologists, is no more than an episode in the critical age, the beginning of one of its phases, the menopause. The whole of the climacteric, with its nervous, circulatory, metabolic and other phenomena, spreads out extensively around about the menstrual phenomenon, beginning prior and continuing after, so that it is extremely difficult to fix exact limits. Long before the appearance of the first vasomotor disturbances and the first irregularities of menstruation, which may be taken as indication that the menopause is beginning, morphologic changes have begun in the individual, such as the development of the heavier and plumper figure and also, perhaps even earlier, those emotional and mental changes which make this period of life so interesting.

And at the other end of the climacteric, at its close, the same condition is true. Menstruation is then over and the great circulatory and nervous upsets, which are so striking, have quieted down. Yet there follow certain anatomic and functional changes dependent on the endocrine imbalance, nor is it possi-

ble for us to say just where these stop, which would give us the starting point of senile transformation. For this reason *it is impossible to reduce to exact dates either the beginning or the duration of the critical age. Only empirically can we say that the most intense phenomena of the crisis are developed between the forty-fifth and the fifty-fifth years.* In Spain the development of menopausal symptoms follows most accurately the statistics of Recasens.^{1, 2}

Some conditions so act on this usual chronology of climacteric disturbances that cessation of the menses, with its symptomatic train, is advanced, *early menopause*, while others delay it, *late menopause*. I believe these states do not merit separate description. The interesting thing about them is not their symptomatology, but the causes which have determined the advance or the delay.

Date of Puberty and Date of Menopause

The laity and many physicians have tried to establish a relation between the time of the appearance of the menses (puberty) and that of their disappearance (menopause). These assume that the earlier puberty came on the earlier also would come the menopause (*prius pubescentis, prius senescent*). *I believe this opinion is incorrect, and its incorrectness lies in the error of assuming a certain and fixed duration for the sexual life.* Naturally, if this were the case an early beginning would involve an early end and vice versa. *On the contrary, the sexual life is of extremely variable duration in women, depending upon the vigor of the ovaries. That is, in women with very active ovaries the sexual life will be long, puberty will be hastened, and the menopause retarded. Contrarily, in those with inactive ovaries puberty will be late and the menopause early, the sexual life short.* The experience of some writers agrees with this point of

¹Recasens: *Ginecologia General*, Madrid, 1913.

²I do not cite here the countless statistics published by writers interested in determining a fixed date for the climacteric, for example:

(a) Künster: *Kurzes Lehrbuch der Gynäkologie*, Jena, 1912, gives forty to forty-two as the date.

(b) Winckel: *Lehrbuch der Frauenkrankheiten*, Leipzig, 1886, forty-eight years.

(c) Scanzoni: *Lehrbuch der Krankheiten der weiblichen Sexualorgane*. Wien, 1907, forty-five to forty-eight. And so on. Later I shall give other opinions,

view, as Raciborski's,³ Brierre de Boismont's,⁴ Guy's,⁵ Kisch's,⁶ Schaeffer's,⁷ Frankel's,⁸ and also my own.

However, it is clear that this statement cannot be taken as an absolute rule in practice, since, as we shall see presently, there are so many circumstances occurring in the course of life which may influence the time limits of the menopause, as diseases or type of sexual life. Consequently it is rare that the ovaries of a climacteric woman retain the functional characteristics which they had at puberty. Thus Novak⁹ could say correctly, "*There is no chronologic relation between the beginning and the end of menstruation.*"

Puberal Pathology and Menopausal Pathology

Notwithstanding this, there are those who call attention to the clinical fact that *menopausal symptomatology presents, in some of its aspects, characteristics similar to those of the puberal symptomatology*. This fact was observed by the classic writers and has been confirmed by Kisch, Tilt,¹⁰ and others. Indeed, in many women similar pathologic states appear in both periods, such as diseases of the skin—eczema, boils, hysterism, asthma, epileptic attacks, recurrent erysipelas and epistaxis. I have observed some such cases referable chiefly to circulatory and psychic disturbances. The explanation is simple. The organs predisposed to pathologic deviation, as the heightened nervous system and the unstable circulatory system, find in both periods analogous moments propitious for their upset. Hence it should not be surprising, although the phenomenon surprised Kisch. These women are likely to weaken at other times, as during pregnancy or the menstrual periods.

³Raciborski: *De la puberté et de l'âge critique dans les femmes*, Paris, 1844.

⁴Brierre de Boismont: *La menstruation considérée dans ses rapports physiologiques et pathologiques*, Paris, 1842.

⁵Guy: *Menstruation*, Med. Times, 1845.

⁶Kisch: *Op. cit.*, note (13), page 19.

⁷Schaeffer: *Die Menstruation*. In *Handbuch der Gynäkologie* Von Veit, ed 3, Wiesbaden, 1908.

⁸Frankel: *Normale und pathologische Sexualphysiologie des Weibes*, Leipzig, 1914.

⁹Novak: *Ueber die Bedeutung des weiblichen Genitales für den Gesamtorganismus*, in *Die Erkrankungen des weiblichen Genitales in Beziehung zur inneren Medizin*, Frankl-Hochwart, Wien and Leipzig, 1912, vol. 1.

¹⁰Tilt: *The Change of Life in Health and Disease*, ed. 5, London, 1870.

Factors Which Influence Climacteric Chronology

We shall now examine quickly the principal factors which alter climacteric chronology. These factors are:

The constitutional energy of the ovary and the structure of the genital apparatus.

The way in which sexual activity has been exercised.

The social condition.

The weight, color of hair, and temperament.

The climate and race.

The state of the previous health, especially lesions of the genital apparatus.

Ovarian and Genital Constitution

It is easy to understand how the sexual decline should occur earlier in women with hypoplastic ovaries and a generally weak genital apparatus than in those endowed with robust generative organs. From this we observe, clinically, an unquestionable relation between the *course of menstruation* and the date of the critical age. Indeed, *women with copious and regular menses tend to lose them later than those whose menses are scanty and irregular*. The quality of menstruation indicates in the first case an energetic ovary and in the second a weak one. Nevertheless, there are cases of profuse menstruation in the presence of an insufficient ovary or thyroid, as we shall soon see. In these cases the crisis is early, naturally. For example:

CASE 2.—B. I., twenty-six years old. First menstruation at thirteen, in northern Spain. After two years of menstrual irregularities the periods became regularly established *but they were profuse*. Various treatments did not succeed in diminishing the hemorrhages. When I saw her I observed distinct symptoms of ovarian and thyroid insufficiency, such as increase in weight, eunuchoid morphology, sterility, extreme sensations of cold, pigmentation around the mouth and on the cheeks, hypogenital hands.¹¹ Ovarian (oocrea) and thyroid extract in

¹¹By *hypogenital hands* I designate a symptom which I have described as very frequent. It is almost constant in women with ovarian insufficiency, especially in young women. It consists of a state of cyanosis, coldness, softness and humidity of the hands, which is subjectively very mortifying to the patient and which gives the observer the same sensation as a hand just taken out of water. (Marañón: Les mains hypogénitales. Revue de Medecine, 1922.)

small doses corrected the hemorrhages and produced a notable improvement in the general state. But four years later, that is, at thirty-one, the menses definitely ceased.

Influence of the Sexual Life on the Advent of the Menopause

The influence of sexual activity on the menopause is also very clear. I shall speak of this later in connection with the quality of climacteric pathology. Here I refer only to its effect on the time of the appearance of the climacteric. This influence can be thus summed up; *celibacy accelerates the menopause*, although sometimes it complicates it. *Its coming is delayed by normal exercise of the genital organs*, regular sexual relations, pregnancies, births and lactations in discreet number and at proper intervals according to the woman's physical resistance. *The menopause can be accelerated by abuses of the genital function*, irregular abuse of cohabitation, frequent pregnancies close together, miscarriage, exhausting lactations. The reason for these differences is easy to understand. In celibate women the ovary reaches its extinction earlier, through the lack of one of its physiologic stimuli. Yet, as I indicated before, and shall explain later at greater length, the disequilibrium during the critical period may be much complicated, in these cases, by nervous influences especially when celibacy has not been voluntary but has been imposed by circumstances.

On the other hand, in the woman who has used her generative ability amply but normally, the ovary has been completely developed and conserves its energy the maximum time,¹² just as a strong man who has made a rational instead of an excessive use of his muscles retains his muscular powers. Norris gives the following explanation of what occurs in the ovary.¹³ Each ovulation gives rise to the formation of white bodies, resembling cicatrices. These accumulate in the cortical substance

¹²For statistics along this line see:

(a) Kisch: Op. cit., note (13), page 19.
 (b) Raciborski: Op. cit., note (3), page 102.
 (c) Cohnstein: Ueber des Klimakterium. Deutsch. Klin., 1873.
 (d) Assmann, in his inaugural dissertation, *Klimax tardia*, Breslau, 1916, gave the following statistics: late menopause as observed by him was presented in 6.8 per cent of nulliparas, 19.42 per cent of oligoparas and 73.79 per cent of multiparas.

¹³Norris: The Menopause, Analysis of Two Hundred Cases. Amer. Jour. of Obst., 1919, vol. lxxix.

of the ovary and may suffice to hinder the development of more follicles. In fact, physiologically, this progressive sclerosis annuls ovarian function in that particular period, the menopause. Now in women who have had several pregnancies, long periods have occurred—as long as the pregnancies—without ovulation and, therefore, without the formation of this cicatricial tissue which conduces to the menopause. On the other hand, this tissue is formed more quickly in nulliparas, in whom the cicatrix is formed month after month without interruption. Premature choking of ovarian function is the end. Furthermore, we should add, in this woman of perfect functional hygiene in her genital life, *the other glands of internal secretion, which are clustered dynamically around the genital, have received in a regular and normal way the stimulus originated in the different sexual experiences. Consequently these other glands help retard the ovarian evolution, as they contribute to the maintenance of entire equilibrium of the individual.*

Finally, in these women whose sexual life has been excessive, the abused ovary has been overworked at the expense of its own structure and is soon exhausted. Fiebag has noted this.¹⁴ A man's muscular system is soon worn out if he works constantly and unhygienically. And, in their turn, the other glands, which cooperate with the genital in the sexual crisis, having also borne an excessive amount of work, are exhausted prematurely. Hence the organism will soon acquire the senile aspect, especially in women predisposed by a debilitated endocrine system. I have observed many cases of this *early menopause accompanied by premature senility* in weak, multiparous women. This state is explicable from the endocrine point of view as due to a *multiple glandular sclerosis*. Basal metabolism tests in these cases give strikingly low figures as Carrasco and I have remarked.¹⁵ The influence of these factors—predisposition and exhaustion—is definitely seen in the following case. Here the menopause began in one of the pregnancies.

CASE 3.—M. de A. Always thin, of short stature and of asthenic constitution; nervous, restless character; emotional;

¹⁴Fiebag: *Klimax precox*. Inaug. Dissert., Breslau, 1911.

¹⁵Marañón et Carrasco, note (16), page 76.

menses normal but profuse; probably a hyperthyroid constitution. Married at nineteen; narrow life. Her husband was an unassuming day-laborer. In sixteen years she had ten children, a number of whom she nursed for some months, and three abortions. At thirty-six she has the appearance of a woman over fifty; shrunken, wrinkled, with all her teeth gone, jaws atrophied, hair sparse and quite white, skin flaccid and full of lines;



Fig. 10.—Premature senility in a multipara of the lower classes. At forty-two the face was faded and lined like that of a much older woman. Note especially the senile atrophy of the jaws with caries and loss of teeth. (Marañón.)

eyesight poor. In a word—this is a typical case of *premature old age*. At this time, coincident with her last pregnancy, the menses definitely ceased without any great functional disturbances, probably representing extinction of the ovary and decreased function of the other glands, especially the hypophysis.

There is an interesting variety of these cases of *premature old age* from multiparity and consequent multiple glandular sclero-

sis. Certain women through the etiology of plain exhaustion acquire the senile aspect, but nevertheless retain menstruation and conceptional power for some years, even beyond the usual age. It would seem as if this particular, purely mechanical part were a veritable "child factory"; as if the genital activity were independent of all the rest of ovarian activity and of the other glands; as if the purely reproductive part of the ovary were isolated from the general sclerosis of the organ. This differentiation of ovarian functions is so possible that there are cases, as we shall see presently, where ovulation persists after the cessation of the menses. Here is an example of this premature old age with persistence of reproductive power:

CASE 4.—S. De C. Forty-seven years old. Always of asthenic type, delicate. Married at twenty-one to a vigorous man. Middle class people. By thirty-five she had borne nine children. Her appearance was that of a woman of fifty: skin flaccid and wrinkled; teeth gone; profoundly asthenic; poor sight; general deterioration; considerable loss of feminine appearance. In this condition she had three more children in eight years. At forty-nine she still menstruated, without evident pathology.

Social Condition and the Critical Age

The social condition also influences the premature appearance of sexual extinction. In these cases which I have described of premature menopause and old age it should be noted that narrowness of social environment, which forces the woman to excessive physical work, collaborates with the simple glandular extinction. Mayer and Payer's statistics, cited by Kisch,¹⁶ show early onset of the menopause in women of the humbler classes. These findings have been generally confirmed by every physician's experience. Mine has been striking and I recall no cases more so than those of the poor women of the lower classes in Castile, particularly those from our most miserable provinces, Avila, Guadalajara and Segovia. These women who came to the clinic at the hospital appeared so aged that I often guessed their age before asking, with the result that they were ten or fifteen years younger than I had supposed. Without a doubt

¹⁶Kisch: Op. cit., note (13), page 19.

the enormous physical difference existing between one of these unfortunates and the youthful freshness, parallel to sexual function, retained by women of abundant economic means is amply explained by the great disparity between their lives. The first have been cruelly lashed by life. The second could concentrate their activity upon the cult of their person, simply because their economic circumstances permitted it. Also these have enjoyed a complete freedom from worry. However, it must not be supposed that it is all a matter of ease. On the contrary, this cult of the body demands long hours of complicated rites which have been perfected from the empiric times of the genial Minon de Lenclos down to the beauty parlors of today which operate under the auspices of science. *Excessive ease, excessive nourishment can, indeed, injure and in fact often do injure sexual function.* It is well known that both of these exogenous factors take part in the production of ovarian insufficiency, and for that reason, in the early production of the menopause. Among oriental women who live in absolute repose, among the women of the harem, among many of the Jewish race, among our society women, among many prostitutes who live very sedentary lives, eating and drinking a great deal, *the obese form of ovarian insufficiency* with premature menopause is frequently observed. Fortunately, in our higher social classes exercise, once banned, is now in more favor and has changed the habits of our women. Yet there are still examples of young women who do nothing but eat, who never exercise, who live a precarious sexual existence and who early become definitely menopausal. No doubt it is for these reasons that in the United States the menopause occurs rather late (forty-six to forty-nine on the average) according to Norris.¹⁷

I am not referring here to the influence of social position upon the *quality* of the menopause. This difference is unquestionable in that among rich women the loss of beauty and of sexual attraction means much more than to the women of the lower classes. These latter usually reach this age worn out and indifferent to their appearance.¹⁸

¹⁷Norris: Op. cit., note (13), page 104.

¹⁸These particularly consider this point:

(a) Icard: *La femme pendant la période menstruelle*, Paris, 1890.

(b) Barbaud et Rouillard: *Troubles et accidents de la ménopause*, Paris, 1895.

Weight, Color of the Hair, Temperament and the Climacteric

Thus we see that all the circumstances just mentioned influence the menopause because they change those previous glandular states which naturally modify the mode of advent of the glandular crisis. The same is true of the rest of the conditions which are cited as influencing the time limits of the critical age. Thus we read "fat women lose their menses before thin ones: blondes before brunettes, phlegmatic temperaments before the sanguine and ardent." (Kisch.¹⁹) These observations, exact but empiric, may be expressed in scientific language: obese women are likely to have a genital or thyroid insufficiency, also, although more rarely, a hypophyseal insufficiency. For this reason they become menopausal early. Hence it would be more exact to say, not that fat women are apt to lose their menses early but women who are prematurely menopausal are apt to be fat. Very dark women are almost always hyperthyroid, hyperpituitary and hyperovarian. Thus the ardent temperament coincides with the dark type. This type fitly symbolizes the popular idea of sexual passion.²⁰ For the same glandular reasons the sexual life is apt to be longer in these than in women with weak ovarian secretions, a condition frequent among blonde and phlegmatic individuals.

Influence of Climate and Race

The same explanation may support the current statement that the *menopause is later in hot countries than in cold*, since the hyperendocrine temperament is much more frequent in proportion as the country approaches the equator. Thus Berchon, cited by Ploss and Bartels,²¹ is certain that the Singhalese become menopausal at sixty. However, it has not been well demonstrated that this is correct. *In Spain, for example, the meno-*

¹⁹Kisch: Op. cit., note (13), page 19.

²⁰"I am ardent. I am dark. I am the symbol of the passions," says one of Bécquer's women with great exactness. Merimée's Carmen, prototype of primitive and blind sexual attraction, was also made, by her creator, dark, active, and nervous. Bizet added a contralto voice, also with true biologic precision, as it belongs to the hyperpituitary temperament. Almost all contraltos present hyperpituitary signs and frequently accompany impetuous sexual energy in women. Recall the profoundly sexual impression made on Gautier, in Spain, on hearing a contralto voice.

²¹Ploss und Bartels: Das Weib in der Natur und Völkerkunde, ed. 10, 1913.

pause is not likely to be later in the warmer regions of Andalusia than in the rest of the country. This is shown by the statistics of the noted and experienced Galvez, of Malaga. This material he was kind enough to give me (oral communication, 1916) and according to it the average age at which the menopause occurs among women of the Andalusian coast varies between the forty-third and the forty-sixth year. This is the same as among the women of the north of Spain.

What is true of Spain may, doubtless, be applied to all other countries. That is to say, in each woman the menopause, like puberty, will depend upon her ovarian potentiality. Upon the latter many individual conditions so act that frequently they annul any influence which climate might have. Artificial circumstances may have a like influence. For example, Stefansson²² has observed that Esquimau women, despite the polar climate, have an early puberty, are mothers sometimes at eleven and it is to be presumed—although he does not say so expressly—that the menopause is also late. This is easily explained by the fact that they live almost constantly inside their houses in an average temperature of 26° C. to 32° C., that is, higher than in the most tropical countries. On the other hand, among the Indian tribes of the northern United States who do not live in such a temperature, but who endure the cold of that region, sexual maturity is late and the menopause early, as classic writers have said. Thus statistics without explanation of conditions are of little value. Consult the writers who have attempted to establish a connection between climacteric chronology and climate and the absolute lack of biologic relation will at once be seen, since the statistical data upon which such connection is based is always arbitrary. It is interesting to note that Raciborski,²³ who is among those most interested in this phase of the problem, gives Norway and Spain as the two nations in which the menopause occurs at extreme ages. Norway is given as a country wherein the menstrual cessation occurs later and Spain as a country where it occurs earlier. According to his statement, the data used concerning Spain were collected by Seco-

²²Stefansson: El factor temperatura en la determinacion de la madurez en los esquimales. Jour. Am. Med. Assn., Spanish ed. 1920, vol. ii.

²³Raciborski: Traité de la menstruation, Paris, 1868.

Baldor, based on studies in Madrid and in the northern provinces of Spain. Raciborski finds himself perplexed by this incongruity which he cannot explain according to his theories. He ingeniously exclaims, "Is this country (Spain) destined to present in all its aspects, the greatest exceptions from our point of view?"

Surely among the destinies of Spain there is no reason to include this one of presenting capricious exceptions to gynecologic rules. I said at the beginning of this chapter that the menopause, in general terms, occurs here at the same time as in other places. What has happened, I suspect, is that the statistics are not correct in these matters which are of great biologic variability. The results of such statistics lead to absurdity. For example, in Raciborski's book, otherwise excellent, these statements appear which I have seen copied many times: "French women become menopausal at forty-six years, three months and seven days; the English at forty-five years and nine months; the Spanish at forty-four" and so on.

Race has little real influence on climacteric time limits. Whatever it might have had, as the expression of an endocrine constitution, is annulled by the other circumstances which I have mentioned. Norris²⁴ and others believe likewise.

Reaction of the Previous State of Health on the Critical Age

Finally *the state of previous health* has an influence on the time when sexual activity ceases. It is evident that the ovarian function is early exhausted in women weakened by chronic diseases. Common observation proves this. It is true of other functions but is even more striking in this case since here it concerns the end and the extinction of a function of *prime importance*. However, among these diseases there are some which have special influence. These are the ones which predominantly affect the functions of the ovary and the other glands of internal secretion. For example, writers say that among chlorotic women the menopause is likely to be premature. We know now that *chlorosis* is a disease linked with disturbances of the ovary,

²⁴Norris: Op. cit., note (13), page 104.

the connection between the two not yet clear but unquestionable. In my opinion the disturbances are probably due to ovarian insufficiency, hence it is not strange that the gland's activity should cease ahead of the normal time.

According to my experience, *syphilis* sometimes causes early menopause through direct lesion of the ovary without the intervention of a general breakdown. This occurred in the following case which I published lately.²⁵

CASE 5.—A healthy, well-nourished, normal woman contracted syphilis in her twentieth year. It was moderately treated and produced scarcely any general manifestations. But a little later the menses ceased completely and a syndrome of extreme ovarian insufficiency developed—early menopause—with such a degree of obesity that it caused death. At autopsy typical lesions were found in the ovaries and an advanced stage of sclerotic degeneration. Microscopic examination confirmed the findings which could certainly be attributed to syphilitic infection localized principally in the genital glands.

Probably *other general infections*, malaria or tuberculosis, could have a like influence, accelerating the climacteric as does syphilis. This would also be especially true of the *local infections*, metritis and parametritis of puerperal, gonorrheal, or like origin, which affect the ovary through contiguity.

Endocrine diseases make up a last series of processes which deeply disturb menopausal onset, hastening it. All these, as is now known, upset the pluriglandular reaction which characterizes the climacteric crisis. Thus, besides qualitatively changing its course, they are likely to advance the time of its appearance. Hence women who suffer from any glandular disturbance, such as Addison's disease, Basedow's disease (although not all), from myxedema, from dystrophia-adiposo-genitalis or from acromegaly are liable to become menopausal early. In the majority of these various cases the ovary is apt to be hypoplastic, as I have shown. Really in many of them one cannot speak of a *true critical age*, since the menstrual function is exhausted early

²⁵Marañón et Bonilla: Un cas d'obésité mortel avec autopsie, Rev. Neurolog., September, 1920.

without the typical reactions of the other glands which are, in my judgment, fundamental to the concept of the *climacteric crisis*.

In cases of *infantilism* the early appearance and symptomatic simplicity of the menstrual cessation is even more marked. As is well known, in many of these infantile women the menses never appear. In others while they appear they are scanty, irregular and ephemeral. They cease very early without other phenomena since the other glands have lost their reactional ability.

On the contrary other pathologic states *retard the menopause*. According to Assmann,²⁶ the diseases which have this retarding action are, in the order of frequency, carcinoma of the uterus, displacements of the uterus, myoma, vulvitis and colpitis, metritis and endometritis, hysteria and lastly Basedow's disease. I do not care to go into the objections which may be made to this order of classification. Regarding Basedow's disease, I would add what I have said before that it sometimes coincides with hypoplastic states of the ovary and therefore with early menopause. But this disease also appears in women with great ovarian potentiality and late menopause. *This type of woman frequently presents early whitening of the hair* as I shall explain presently at greater length. For the present I may say that there is an unquestionable relation between these three phenomena, *early whitening of the hair, hyperthyroidism and late menopause*, although it cannot yet be well explained.

False and True Late Menopause

I cannot stop reiterating the important fact *that not all cases described as "late menopause" merit the name*. There are, indeed, a considerable number of women with "true tardy menopause," that is, women over fifty who continue menstruating normally for some time. I have seen one patient in whom *authentic* menopause occurred at sixty. Renaudin reported one which occurred at sixty-one; Schuler another at sixty-two; Mayer three at sixty-four; Courty one at sixty-five; Baigel an-

²⁶Assmann; Op. cit., note (12d), page 104.

other at the same age; Donizetti one at seventy-nine and Raciborski recalls a case "cited in the *Memoires of the Academy of Sciences* of 1778," of a woman aged one hundred and six who still menstruated.²⁷

But on the other hand, many of these cases of apparent menstruation abnormally prolonged are simply cases of *postmenopausal periodic hemorrhages*, which have nothing to do with ovulation. Sometimes there are uterine lesions, incipient cancers principally, which cause the persistence of the flow. Also there are the frequent myomatous states, metritis, endometritis and uterine displacements; in short almost all the cases given by Assmann as unequivocally *klimax tarda* in the table I copied not long ago. Again, although more rarely, the hemorrhages persist, with more or less periodicity, but without ovulation and without any genital lesions disclosed by the most careful examination to explain them. Even here there may be some small and benign lesion which escaped detection and can only be found at autopsy. This occurred in Seanzoni's case, cited by Kisch,²⁸ of a woman sixty-one years old with monthly hemorrhages which were taken for persistent menstruation. She died of pneumonia and at autopsy two small polypi were found in the neck of the womb. The ovaries were atrophied.

Again, there is no lesion, diagnosticable or overlooked, to which the hemorrhages may be attributed. Nor are they due to an abnormal persistence of ovulation, but to a *dyscrasic state*, a *tendency to hemorrhage*, perhaps related to insufficiency of the thyroid. I have seen this demonstrated in several cases which I shall discuss later. Finally, recent writers include under the term *myopathic hemorrhage*, a group of patients with profuse and prolonged uterine hemorrhages. These, while lacking the usual changes in the genital apparatus or general processes to which the bleeding may be attributed, have been interpreted as the consequence of a particular uterine state.²⁹

In short, *we should not make a diagnosis of late climacteric unless all such lesions as have been mentioned can be ruled out, as*

²⁷See the bibliography in Kisch., op. cit., note (13), page 19: Tilt, note (10), page 102: Raciborski, note (3), page 102: Assmann, note (12d), page 104, and Ploss und Bartels, note (21), page 109.

²⁸Kisch: Op. cit., note (13), page 19.

²⁹In the next chapter I shall consider these points in greater detail.

these independently of ovulation can prolong the appearance of the uterine flow. A diagnostic error in some of these cases, that of incipient cancer, can entail irreparable injury to the patient.

Postclimacteric Conception

Cases of *postclimacteric conception* are of great biologic interest. The oldest known case is that of Sarah, wife of Abraham.³⁰

Brandt³¹ cites the five following cases collected from the literature; Priou's case, menopause at the forty-eighth year and a two months' abortion at the sixty-second year; Levasseur's, menopause at the fiftieth year and delivery at the fifty-second; Underhill's, menopause at the forty-ninth and delivery at the fifty-first; Depasse's, menopause at the fifty-ninth year and delivery at the sixty-eighth; Hahn's, delivery three years after menopause. I shall add one from my experience where delivery occurred three years after a normal menopause. The child was achondroplastic. Lactation was normal and the menses reappeared.

Cases of young women with ovarian insufficiency and complete absence of the hemorrhagic phenomenon of menstruation who, nevertheless, become pregnant are relatively frequent. I have seen several. The same explanation serves for these and for those with postclimacteric conception, that is, a silent ovulation, insufficient to give rise to the hemorrhagic reaction but adequate none the less to produce an ovum capable of fertilization.

Duration of the Crisis

As both the beginning and the end of the critical age depend on such diverse factors, it is easy to understand how exact figures

³⁰*Genesis* Chapt. xviii: 10. Sarah thy wife shall have a son. And Sarah heard it in the tent door, which was behind him. 11. Now Abraham and Sarah were old and well stricken in age; and it had ceased to be with Sarah after the manner of women. 12. Therefore Sarah laughed within herself, saying, After I am waxed old shall I have pleasure, my lord being old also? 13. And the Lord said unto Abraham, Wherefore did Sarah laugh, saying Shall I of a surety bear a child, who am old? 14. Is anything too hard for the Lord?

Chapt. xxi: 2. For Sarah conceived, and bare Abraham a son in his old age, at the set time of which the Lord had spoken to him. 5. And Abraham was a hundred years old when his son Isaac was born unto him. 6. And Sarah said, God hath made me to laugh; so that all that hear will laugh with me. 7. And she said, Who would have said unto Abraham, that Sarah should have given children suck? for I have borne him a son in his old age.

³¹Brandt: *Pregnancy after Menopause*, New York Jour. and Med. Rec., 1922, cxvi, No. 1.

can scarcely be given for the *duration* of this stage of life. Kisch³² gives two or three years as the average. In the greater part of Tilt's cases³³ it lasted approximately one year. Norris³⁴ gives the same period adding that when the menopause exceeds this limit it should be considered as pathologic. I am inclined to accept the more ample figures given by Kisch. I believe, in the majority of cases, *including the first symptoms of the crisis and their prolongation after the cessation of the menstrual flow, the menopausal crisis occupies much time—two years, three, or more—in the evolution of feminine life*. From this complex of phenomena the most striking and interesting may be isolated, as those which coincide with the menstrual upset. These really occupy approximately one year. Doubtless it is to this culminating, central, but partial section of the curve described by the endocrine crisis of the climacteric to which Norris and Tilt's figures refer.

Therefore, I believe it is impossible to fix mathematically (as Norris does) a period of duration for the normal crisis, beyond which it should be considered pathologic. [Inasmuch as uterine malignancy is so often overlooked by the general practitioner and because it is characterized by irregular bleeding, anything suggesting malignancy must be looked upon with suspicion. Some writers, Watkins among them, have argued that any excessive, or unexpected bleeding, during the climacteric years should be regarded as evidence of potential malignancy. It is for this reason, one of propaganda in the prophylaxis of cancer, that emphasis is placed on long duration of time as covering the menopause in its entirety.—C. C.]

The sexual quenching is briefest in women with infantilism. Nevertheless it is pathologic. On the other hand, very strong women with vigorous ovaries and endocrine systems may pass many years in the change without any scientific reason to justify us in considering them pathologic.

³²Kisch: Op. cit., note (13), page 19.

³³Tilt: Op. cit., note (10), page 102.

³⁴Norris: Op. cit., note (13), page 104.

CHAPTER XI

GENITAL SYMPTOMS

Classification of Climacteric Symptomatology

The climacteric symptoms can be divided into as many groups as there are apparatus in the body because they all can be affected in the crisis. *Those symptoms which are found with greater frequency are:* (1) *genital*, (2) *circulatory*, (3) *nervous*, (4) *metabolic*, (5) *endocrine*, (6) *digestive*, (7) *cutaneous* and finally (8) *symptoms of other organs and apparatus*.¹

The genital symptoms, which are the most interesting to the gynecologist, are for me rather less so than the circulatory and the nervous, for example. Until the present time these genital symptoms constituted the central element in the classic concept of the menopause. In this monograph I have striven to supplant them with other more extensive symptoms which are of greater pathologic foundation.

Behavior of Menstruation

The most important manifestation of the first symptomatic group is the *behavior of menstruation*. Physiologically this consists of a gradual diminution of the menstrual flow so that, in a few months, it ceases altogether without any disagreeable variations. But such a smooth transition is rare since it presupposes a perfect anatomic and functional integrity of the endocrine-vegetative system, a degree of perfection almost impossible to conserve past the fortieth year.

*Vinay's statement*²—that “more than 50 per cent of women” have a regular and progressive withdrawal of the menses seems to

¹According to Barie—*Etude sur la Menopause*, Paris, 1874—this is not the order of frequency of the menopausal symptoms. According to his statistics, which included 3,243 women, they presented: 1,678 nervous symptoms, 705 cutaneous symptoms; 463 respiratory symptoms; 354 symptoms of the digestive tract; and 43 symptoms on the part of other apparatus. Note in this classification the absence of the most frequent and interesting circulatory symptoms. No doubt Barie included these among the nervous.

²Vinay: *Op. cit.*, note (12), page 19.

me glaringly exaggerated. In the majority of cases the disappearance of the menstrual flow is accomplished in a much more irregular way. According to Tilt's statistics,³ of 637 women, in twenty-six the menses withdrew by slow degrees; in 14 per cent, suddenly, and the rest suffered metrorrhagias, single or multiple at varying intervals. Within the last group hemorrhagic menstruation repeated at intervals of more than twenty-one days was the most frequent form. Kisch's statistics⁴ give 57 per cent as having climacteric hemorrhages.

Climacteric Hemorrhages

Therefore, hemorrhage is the predominant local phenomenon of the climacteric. My experience in this respect agrees with that of all observers. Description of the symptom is unnecessary as it is a phenomenon of common note. Sometimes it begins with the first climacteric upset, the excessive menstruation being the initial symptom of the crisis. Again, it occurs several months after other menstrual disturbances. Sometimes the hemorrhages are presented regularly, keeping the same rhythm as normal menstruation. Or they may appear at longer or even shorter intervals than usual in that particular woman. The amount of blood lost can be sensibly perceived in each period to be either diminishing gradually from the first, or increasing up to a certain time and decreasing thereafter. Or profuse menses may be presented alternately, or irregularly, with scanty periods. Usually the interhemorrhagic intervals finally lengthen and two or three months may elapse without menstruation, or but slight traces, to be suddenly broken by another hemorrhage, at times much more copious. Another period of rest ensues, followed in turn, after some months, by further hemorrhage. This continues until definite menstrual suppression occurs.

Even after this suppression women frequently continue to experience the same or similar local and general distresses, which used to accompany menstruation, in the days corresponding to the period. They also are more strongly aware of a subjective menstrual sensation in the amenorrheic intervals at the beginning of the crisis.

³Tilt: Op. cit., note (10), page 102.

⁴Kisch: Op. cit., note (13), page 19.

Involutorial Chlorosis

In general these hemorrhages, even though they be very profuse, are not apt to disturb greatly the general state of the patient's health. She quickly recovers from the loss of blood. *But sometimes the hemorrhages do reach the point where anemic states are established. In my experience this occurs only, or at least becomes grave only, in those women whose hematopoietic state was previously weak.* The cases so affected are chiefly those which presented chlorotic manifestations at puberty, the trouble, as usual, ceasing as the genital sphere reached maturity. In these cases the menopause is apt to be accompanied by profuse hemorrhages, as I have already indicated, and chlorotic symptomatology not rarely recurs. I have seen many cases of this *late chlorosis, or chlorosis of involution*, the symptoms of which reproduce those of ordinary chlorosis, such as greenish pallor, various digestive and nervous upsets, and typical hematic changes. From the therapeutic point of view, late chlorosis, like the true chlorosis of puberty, is benefited more by ovarian therapy given with the usual preparations of iron and arsenic than by such medication alone.⁵

Posthemorrhagic Nervous Depression

In other patients the profuse hemorrhages do not cause anemic disturbances but *produce states of nervous depression. These are aggravated during the hemorrhage up to the point of apprehension amounting to terror*, as in some of my patients.

CASE 6.—A woman of forty-seven years; always delicate and timid; menopause characterized by abundant hemorrhages. She had heard of a woman who died of such a hemorrhage, and the appearance of the flow caused an extraordinary terror. She remained in bed during the entire flow without moving, being fed by a tube and not venturing to breathe deeply in order not to

⁵Let me note the fact, pointed out recently by various French and North American writers, of the disappearance of chlorotic states in those countries. I have elsewhere expressed my opinion that while typical chlorosis, which was always a rare disease, has indeed disappeared, on the other hand we continue to see a great many cases of a typical chlorosis, of anemic states without all the characteristics of that disease but presenting an indubitable clinical unity. Note, previously cited, (11), page 54: Fiessinger and Bidereray express a similar opinion. *La chlorose est devenue une maladie exceptionnelle. Jour. des Pratic.*, March, 1924.

increase the amount of blood lost. She kept her eyes closed while changing napkins so as not to see the amount of the hemorrhage. One day in a theater, she felt that menstruation was beginning, and she suffered an emotional faint. While the hemorrhages were profuse, they were not in the least dangerous, and did not affect her general health in any way.

Pathogenesis of Climacteric Metrorrhagias. Metrorrhagia, Symptom of Uterine Cancer

The *pathogenesis of these hemorrhages* interests me greatly. Until the last few years every hemorrhage which coincided with the critical years was considered as a natural consequence of the age and was not given much importance, the *essential metrorrhagia of classic writers*.⁶ It was only after these women, with supposedly harmless hemorrhages, had been observed for months or years that a reaction set in against this light way of looking at this symptom. Gynecologists repeatedly found that, on examination, there was a uterine neoplasm, usually a fibromyoma or a fully developed cancer. Then followed an era of propaganda in which the gynecologist called attention to the pathologic reason for excessive bleeding, emphasizing the fact that, *whether scanty or unaccompanied by local distress and disturbances of the general health, they were often the initial manifestation of uterine cancer whose sole hope of treatment lay in early diagnosis*.

Undoubtedly the diffusion of these facts in Spain by Recasens,⁷ by Vital Aza⁸ and others has been valuable to many women. Even exaggerations should perhaps be accepted as a good thing in propaganda. But it is certain that the anatomic interpretation of these hemorrhagic states has been carried a little too far when they are considered in every case as syndromes of uterine lesion. Indeed, *the investigations of these last few years have demonstrated that a large group of the hemorrhages in the critical age are produced without inflammatory or neoplastic lesion in the*

⁶On the classic conception of the medical hemorrhages of the menopause see Stopin: *Essai sur les metrorragies de la Menopause*, Paris, 1898.

⁷Recasens: *Op. cit.*, note (1), page 101.

⁸Vital Aza: *Falsos diagnósticos endocrinos*. C. a la Real Academia de Medicina de Madrid, March, 1924.

uterus. Their origin should be sought in the disturbances of the internal secretion of the ovary, and perhaps of the other glands which take part in the menopausal crisis. Excessive bleeding may be due to other extragenital pathologic conditions such as the woman's circulatory state; or they may be due to those poorly defined pathogenic changes which writers designate as hemorrhagic metropathies. These I shall describe presently in more detail. Still it is prudent to continue to consider these states as relatively exceptional, as diagnoses which are to be reached only after carefully eliminating the possibility of benign or malignant uterine tumor.

But, this proviso made, let us see how we may explain the hemorrhagic disturbances in those cases in which no anatomic reason, either inflammatory, or neoplastic, can be found. There are cases in which neither the most careful examination by an expert using the most recent technic, nor the further evolution of the trouble gives any hint as to the cause.

Are Metrorrhagias Due to Hyperoöphorism?

We must first consider the hypothesis which Pende,⁹ Novak,¹⁰ and others offer that these hemorrhages in some cases may be the expression of a state of hyperfunction in the ovary, hyperoöphorism. I have already said (page 36) that in my opinion this premenopausal hyperoöphorism does not occur as a constant phenomenon. Based on observation in certain girls and young women in whom puberty occurred early and the primary and secondary sex characteristics were markedly developed, cases of true hyperoöphorism, my experience has taught me that while the menses in such individuals are energetic they are not pathologically hemorrhagic.

Are There Hemorrhages Due to Ovarian Insufficiency Properly Speaking?

Earlier (page 29) the studies of Seitz and his school were cited. These attained a vogue which was even reflected in the first edition of this book. According to these studies the corpus

⁹Pende: Op. cit., note (17), page 19.

¹⁰Novak: Op. cit., note (17c), page 29,

luteum elaborates, let us recall it once more, two sets of hormones. One is developed early, of proteinic nature (lipamine) which brings on the menstrual change in the uterine mucosa and therefore provokes the menstrual flow. Another set developed later, of lipid nature (luteolipoid) causes the involution of the uterine mucosa and consequently the cessation of the menses. According to this theory it may be assumed that as insufficiency of the first group of hormones might give rise to scantiness or absence of the menstrual flow, so insufficiency of the hormones in the second group might cause, on the contrary, a profuse and persistent menstrual hemorrhage through the lack of its physiologic curb. *Thus there might be excessive bleeding due to ovarian insufficiency properly speaking.*

Some clinical facts seem to support the probability of this hypothesis, as I noted in the first edition. That is, these hemorrhages appear to be relieved by ovarian preparations which are rich in the supposed lipid hormones. However, a stricter and fuller examination of my patients has led me to a conclusion which rectifies my first impression. I now believe that *these hemorrhages from hypo-ööphorism are merely hypothetic* and are not confirmed clinically nor by experimentation. Hence it is not strictly correct to speak, as Lauth does,¹¹ of "ovarial hemorrhages." However, the hypothesis stands for future proof.

Hemorrhagic Metropathy

Yet, as I indicated, there are cases of uterine hemorrhages in the critical age wherein the disturbance, if not purely functional is at least so mild from the anatomicopathologic point of view, that it can be relieved by purely medical or physical means, or even spontaneously. These immediately justify a benign prognosis. We have all seen innumerable cases belonging to this group and to which, at least in part, can be applied the diagnosis and explanation proposed by such men as Schroeder,¹²

¹¹Lauth, G.: Ueber das Verhalten des Uterus bei ovariellen Blutungen, Monatsch. für Geburtsh. und Gynäk., 1915, xlii, 19. Along this line see Guíllera's interesting article Contribusio a l'estudi de la metropatia hemorrágica. Treballs de la Soc. de Biol. de Barcelona, 1917.

¹²Schroeder: Die Pathogenie der Meno- und besonders der Metrorrhagien. Monatsch. f. Geburtsh. u. Gynäk., 1920, li.

Pankow,¹³ and Evans,¹⁴ under the name *hemorrhagic metropathy*.¹⁵ The fundamental symptoms are: first, profuse hemorrhages without a cyclic course—that is without relation to the menstrual rhythm and not infrequently appearing after a more or less prolonged period of amenorrhea; second, the endometrium is hyperplastic but without the signs of premenstrual edema; and third, no recent ovulation, therefore, no recent corpora lutea, but there are persistent follicles apparently mature.

Probably the endometric disturbance and the hemorrhage are due to this condition in the ovary. Evans insists on this and cites other writers in his support. Indeed, everything appears to indicate that, explained in one way or another, there are climacteric hemorrhages which correspond to phases of endocrine function in the ovary, but these phases are not well understood. Nevertheless the hemorrhages are not due to a pure hyperfunction nor to a pure hypofunction. It is important for the physician to know that such hemorrhages do exist.

Influence of Coagulating and Anticoagulating Hormones

Writers upon the subject of these hemorrhages have persistently forgotten a factor which is important although not yet clear. I refer to the *participation of the endocrine glands in certain disturbances of the coagulability of the blood*, an influence which makes the latter flow exaggeratedly on leaving the circulatory apparatus, as occurs in hemophilia. We might say that the endocrine crisis of the menopause is capable of causing just such "mild hemophilic states." Ovarian extracts have at certain times coagulating properties (Kintsi) or anticoagulating (Schickele¹⁶), (Adler¹⁷), a fact which perhaps should be interpreted more as mere experimental phenomena and not as the expression of physiologic properties of the corresponding internal secretion.

¹³Pankow: Die Metropathia haemorrhagica. Ztschr. f. Geburtsh. u. Gynäk. 1912, lxx.

¹⁴Evans: Op. cit., note (17b), page 29.

¹⁵Novak: Op. cit., note (17c), page 29, gives to these cases the name "functional uterine hemorrhage." This does not appear to me to be entirely exact, since the adjective "functional" seems to exclude every lesion of the uterus.

¹⁶Schickele: Op. cit., note (14), page 19.

¹⁷Adler: Op. cit., note (28), page 62.

But, apart from the ovary, another gland which constantly intervenes in the climacteric, the thyroid, acts definitely on the blood crasis. Indeed, it also behaves in a paradoxical manner, for I have seen numerous cases of hyperthyroidism with retarded coagulation. Surgeons are familiar with this, since in goiter operations they sometimes have to struggle with blood which is difficult to control. On the other hand, I have seen cases of hypothyroidism (cretinism) with a grave decrease in coagulability. This I am now studying with Bonilla.¹⁸ *It is, then, not venturesome to suppose that the thyroid, the ovary, and perhaps some of the other glands intervening in the menopause when they depart from the normal, may produce deficient coagulability, thus favoring the production of menstrual hemorrhage.*¹⁹

Influence of Climacteric Hypertension on Uterine Hemorrhage

Finally, *high blood pressure, so constant and at times so marked in the critical age, doubtless acts on the pathogeny of the phenomenon* we have just been considering. It operates, doubtless, on a secondary plane. While a coincidence of profuse hemorrhage in women with extreme hypertension is frequently observed, this is not always the case. I have seen several instances of intense climacteric hemorrhage in delicate and asthenic women with proved hypotension. A case in point is the following:

CASE 7.—Woman of fifty-two; always asthenic, delicate, general visceral ptosis; multipara; severe asthenia; pulse “always weak.” Menopause complicated by *severe hemorrhages* and various disturbances of vasomotor type. Oscillometric determination gave no figures higher than 11, maximum tension.

¹⁸My collaborator M. Izquierdo has published a case from our clinic. Un caso de insuficiencia tiroidea con hemorragias uterinas. *Anales de la Academia Medico-Quirungica*, Madrid, 1922-23. This concerned a young girl with grave uterine hemorrhage rebellious to all gynecologic treatment. On diagnosing thyroid insufficiency and giving thyroid therapy we succeeded in stopping the hemorrhage immediately. The same may be true of some climacteric women.

¹⁹These glands act on coagulation, doubtless through their well-demonstrated intervention in calcium metabolism, since calcium equilibrium is a fundamental factor in good blood crasis. Upon this point of the treatment of diseases of the bones in their relation to the glands of internal secretion I have collected a vast amount of data and cases. These appear in my volumes *Enfermedades de la nutrición y glándulas de secreción interna*, Third edition, Madrid, 1919.

Other Menstrual Disturbances of the Climacteric

The above data which explain the production of the hemorrhages also explain the other disturbances of menstruation, such as the *gradual diminution of the menstrual flow*, corresponding to gradual parallel suppression of the internal secretion of the ovary; likewise is explained the *intermittencies of menstruation* which are due to a decline, also undulating and intermittent, of the endocrine impulse.

Abrupt Menopause

Hemorrhage, gradual diminution or intermittency, are the three usual clinical modes of menstrual disturbance. *Abrupt menopause* appears less often.

In abrupt menopause, as its name implies, things so happen that suddenly, without menstrual antecedents in the preceding months, the menses stop and never appear again. Generally this abnormality is produced by the sudden, abrupt and intense influence of one of the various factors which we have considered in the preceding chapters as intervening in the etiology of pathologic menopause. For example, cases are relatively frequent wherein the sudden suppression of the menses coincided with some serious infection, as typhoid fever in two of my cases, exanthematous typhus in another case, or cholera, as in three of Courti's cases.

Even more often examples of this abrupt menopause are seen as a consequence of intense emotion. Numerous cases are found in the literature. Krieger reports one of a woman whose menses ceased definitely on learning that her husband had died. Brierre de Boismont gives another in whom sudden menopause occurred when her house burned. Along with all physicians I have seen such cases, referable principally to grave emotional states produced by the death of a loved one, especially a husband, in certain passionate women. It is as if to the generic factor of the emotion a specific psychic factor had been added. Thus in my cases this phenomenon coincided with the conviction that any future love would be impossible. These instances of menopause of emotional origin are easily understood through a study of the mechanism of emotion which I explained farther back. There

we saw that the emotion caused a neuroendocrine disturbance which either by its violence or reacting on a predisposed woman might give rise to sudden and permanent inhibition of ovarian activity.

Cases are also cited of abrupt menopause consequent to losses of blood, as hemorrhoidal hemorrhage (Disourd), bleeding (Tilt); severe traumatisms, a fall downstairs (Kisch); to hysteric attacks (Krieger); labor (Brierre de Boismont, Meyer and myself²⁰). In many of these cases the intervention of the emotional factor is probable. Besides this, the general weakness and ovarian weakness together with the other circumstances which we have studied also have an influence.

Anatomic Changes in the Genital Apparatus During the Menopause

The foregoing symptoms, functional manifestations of genital decadence *are accompanied by corresponding morphologic changes in the sexual apparatus*. I have already described those occurring in the *ovary* (Chapter II). The *uterus* enlarges slightly at first, because of the congestive influence to which it is subjected. Later it undergoes a progressive shrinking, which begins at the cervix and goes on to the corpus. This shrinking continues up to senile atrophy. The glands of the cervical mucosa tend to become transformed into cysts, the so-called Nabothian follicles.²¹

The *vagina* becomes flaccid. Its mucosa appears bright red and frequently full of secretion. Later its walls harden and dry out when the erethistic phase of the crisis has calmed down and senile quenching is initiated.

A congested state is observed in the *external genitals*, at the beginning. This is sometimes very marked and coincident with local neuroses, such as pruritus. Later the fat in the *mons veneris* disappearing, it flattens. The labia majora become flaccid and separate, as do the labia minora and both darken in color.

It is an interesting and characteristic *fact that the hair on the mons veneris uncurls*, becoming straight in this age. In connec-

²⁰See the bibliographies in the general works by Kisch, Vinay, etc., for data on these cases.

²¹See the excellent article *Estudio histológico de las alteraciones de la mucosa uterina en la menopausia*, by P. Rey y Baltar, *Galicia Medica*, November, 1918.

tion with this phenomenon we may recall the observation of the sexual impulse causing curled hair, in both man and woman, especially in certain mentalities of elemental sexuality and little delicacy.

Leucorrhea

All the above is in the normal menopause. Entering now into the decidedly pathologic field, let me state in the first place, that a great number of menopausal women present one symptom which may become distressing—*leucorrhea*. In general it is an indication of inflammatory lesions of the genitals, as endometritis, vaginitis or vulvitis. But sometimes it is presented in periodic form without other symptoms and without further consequence. It may then be accepted as a phenomenon of vicarious significance. According to my experience this is rather frequent. In Kisch's²² statistics it appears in more than 50 per cent of his observations.

Inflammatory and Neoplastic Lesions

Here leucorrhea is a frankly pathologic character—indicating *the inflammatory and neoplastic lesions*, which I shall now consider briefly. Regarding the so-called *genital neuroses*, which are usually studied in connection with the former, I shall mention them in the chapter on nervous disturbances.

It is true, as I said before, that hemorrhages which appear clinically benign may mask the beginning of a uterine affection. Hence, let me repeat, *the internist should insist on an early gynecologic examination at the least suspicion that some such lesion may be causing the persistence of the hemorrhages or other local and genital symptoms*. In general, when these lesions are really present, the hemorrhage acquires well-known characteristics. These are lack of periodicity, intermenstrual spotting, characteristic aspect and odor of the discharge and of the bloody or leucorrheal ooze which is apt to follow the hemorrhage. Especially significant is the presence of local distress and disturbances of the general health. Any of these immediately place the patient in the gynecologic field. While the hemorrhages *sometimes* do

²²Kisch: Op. cit., note (13), page 19.

not appear at all suspicious, yet they may be due to grave organic lesions and the practitioner should never forget this.

In this medical study we shall not take up the details of these gynecologic diseases, since their exact diagnosis and their treatment do not concern the internist. I shall mention only the fact that the following appear in this age or are aggravated; *metritis* and *endometritis*, of varying intensity and symptomatology; *uterine displacements*, principally prolapsus (65 per cent of Kisch's menopausal cases), which may precede the crisis and be merely accentuated by it; and finally *uterine tumors*²³ which are one of the most dangerous reefs at this period of life and merit some comment by themselves.

We must distinguish between *benign tumors* (*myomas*, *fibromas*) and *malignant tumors* (*carcinomas*). Uterine myomas and fibromas do not elect this age for the time of their appearance, as some believe. These tumors are frequently unnoticed by the patient until the symptoms, particularly the hemorrhages, increase and become marked in the climacteric. *The essential thing for the physician is to know that a fibroma may be the cause of hemorrhage in the menopause acquiring an abnormal intensity or an atypical course, and that in the case of a woman who is not yet menopausal but who has one of these tumors the crisis will probably be later than in the normal woman*, as I said before. In many cases the tumor involutes favorably after the menopause, atrophying and finally disappearing. Hence it used to be the accepted rule in the treatment of these tumors to look forward to the menopause in the hope of a spontaneous cure. Now gynecologists insist that in such cases watchful waiting increases the chances of an unfavorable course, especially because of the possibility of malignancy. For all of these reasons even those who are not specialists, having had sad experience, advise the use of active treatment from the very moment of diagnosis. [The gynecologist sees too many patients build false hopes on this belief and neglect a growth that might easily be cured until complications have rendered operation more dangerous. Our experience is that only rarely, indeed, does a fibroid growth disappear. The

²³I do not wish to omit mentioning the cancers of the other parts of the genital apparatus, also frequent in this age, as, for example, vulvar cancer. This has recently been well studied by Stajano (*Estudio clínico del cáncer vulvar*, Rev. Med. del Uruguay, 1919, y *El precancer vulvar*, *ibid.*)

great majority either remain without symptoms or with gradually increasing symptomatology. I have seen cases in which the symptoms bringing the patient for treatment appeared after the climacteric years, occasionally even with continued increase in the size of the tumor.—C. C.]

According to Recasens,²⁴ the internal ovarian secretion is influential in the production of muscular tumors of the uterus. This hypothesis is based on the abnormally large size which the ovaries acquire in these cases, and while this fact used to be explained as a change secondary to the myoma, he now assumes that the hypertrophic ovaries represent states of primary ovarian activity which cause a secondary uterine reaction. Various histologic and therapeutic studies have confirmed this hypothesis of "primary hyperoöphorism as a cause of myoma." This easily explains the fact that the menopause in causing the function of the ovary to cease also causes the myoma to disappear.²⁵

In regard to *carcinoma* the frequency with which its appearance coincides with the menopause is incontestible. This remark includes everything that can be said on the relation between the two states. "The appearance of uterine carcinoma," says Recasens, "is a phenomenon dependent upon the conditions which present themselves in the individual between the fortieth and the sixtieth years; but it is not an effect of them." *I would go further, beyond the cases which are really suspicious, and I would suspect cancer in the first symptoms which gave any doubt as to the endocrine origin of the flow*, in order to give physical or surgical therapy time to act with some chance of success in those cases where a specialist's examination confirmed my suspicion.²⁶

Vicarious Hemorrhages

In addition to the genital aspects just enumerated, let me mention one very curious menopausal manifestation, *vicarious hemorrhages*. This well-known term corresponds to certain cases

²⁴Recasens: Op. cit., note (1), page 101.

²⁵Hegar and other writers have made fibromyoma of the uterus depend upon previous ovarian changes. But they assumed that these lesions were hypofunctional. In this respect see Luncz: *L'opotherapie mammaire dans les hemorrhagies et dans le fibrome de l'uterus*, Paris, 1911.

²⁶For a detailed study of these states of the genital organs in the menopause see Tilt, Vinay, Kisch, Recasens, etc., so frequently cited in these pages.

wherein, after the withdrawal of the menses, a menses-like flow of blood, of greater or less amount, continues from some other part of the body than the genital tract.

The commonest expression of this vicarious bleeding is *hemorrhoidal hemorrhage*: after this there comes in approximate order of frequency, *epistaxis*, *high intestinal hemorrhages* (*melena*), *hematemesis*, *hemoptysis* and finally rare cases of *mammary hemorrhage*.

Pathogenesis of Vicarious Hemorrhage

I am especially interested in making clear the significance of this phenomenon from the pathogenetic, diagnostic, and prognostic points of view. In my judgment, *this is always a pathologic phenomenon* and should receive careful investigation before adjudging it lightly as the mere substitute for the uterine hemorrhage, and giving it a benign prognosis.

In a general way, two factors intervene in the pathogenesis of this symptom. On one side we have the general circulatory state, characterized by hypertension, which is an almost constant phenomenon in the menopause, and vasomotor fluctuations which predispose to local congestions. Both factors are exacerbated during the days of menstruation. On the other hand, *a point of lowered resistance* must be admitted—and on this rests the pathologic character of these hemorrhages—represented by some previous lesion, generally hidden. Through this weaker point the blood finds easy exit when subjected to pressure. *Now this previous lesion may be benign or malignant and this is what must be decided in order to give the symptom its proper prognostic value.*

Rectal Hemorrhages

Rectal hemorrhages deserve a benign prognosis more frequently, since they almost always originate in hemorrhoidal lesions. Their rupture, because of general circulatory changes, is a common accident. Every writer cites cases of this kind. Among 500 menopausal women Tilt²⁷ found:

In 60 cases, simple nonbleeding hemorrhoids.

In 24 cases, hemorrhoidal hemorrhages without rhythm.

²⁷Tilt: Op. cit., note (10), page 102.

In 1 case, rhythmic hemorrhoidal hemorrhages.

Nevertheless, one should be on guard against the possibility of the discharge originating in a carcinoma, either of the rectum or of the sigmoid flexure. Occasionally cancer may develop here a long time without great subjective symptoms (Wagner²⁸). For this reason a proctoscopic examination should be made whenever the intensity or the frequency of the hemorrhages, or better the presence of other suspicious symptoms, invite doubt. Such symptoms are loss of weight, lack of appetite, sallow appearance and local distress. When neoplastic lesions are not apparent the proctoscope may show the intestinal mucosa filled with a fine close net of engorged vessels whose rupture causes the bleeding. Again, if no change is observed in the mucosa a parenchymatous capillary hemorrhage must be admitted (Singer²⁹).

Epistaxis

Cases of vicarious *epistaxis* are rare and their significance is likely to be benign. I observed a case of this in a woman who all her life had bled easily from the nose. This caused me to suspect the existence of a local lesion in the nasal mucosa which the specialist's examination confirmed.

Melena

High intestinal hemorrhage (melena) is also observed with this vicarious character sometimes. Tilt found it in twenty-two cases out of 500 menopausal women, twenty without the character of periodicity and two periodic, monthly. I believe one should always be cautious in its prognosis, because of the possibility of its being the first manifestations of a malignant process, since this age is propitious for such development. In this connection I cite the following case which is interesting because all conditions appeared favorable.

CASE 8.—A woman of forty-eight; always well but very nervous. After a rapid menopause she presented high intestinal hemorrhages (*melena*) monthly accompanied by subjective dis-

²⁸Wagner: Digestionstrakt, in *Die Erkrankungen des weiblichen Genitales in Beziehung zur inneren Medizin*: Frankl-Hochwart, i. Wien u. Leipzig, 1912.

²⁹Singer: *Darmerkrankungen in Klimakterium*, Med. Klin., 1908.

tress similar to that felt during menstruation. She had extreme hypertension—21 maximum, 11 minimum. General health and appetite good. Examination of digestive apparatus negative; analysis of stomach normal. Some colicky distress, infrequent and not very intense. Various physicians diagnosed this as *vicarious intestinal hemorrhage*. I did so myself, although making a reservation as to the nature of the bleeding lesion. I saw her again in six months. She was now thin, pale, and in great pain. The proper menopausal symptoms had disappeared. The hemorrhages were farther apart and had lost their periodicity. Palpation revealed the existence of an extensive swelling in the abdomen, below the umbilicus, painful, with involvement of the inguinal glands. The diagnosis of intestinal cancer was later confirmed by the rapid progress of the disease and by the development of the tumor. Without doubt in this case the earliest phases of the neoplasm, which are ordinarily unnoticed by the patient, were revealed by the hemorrhages, provoked in situ, through the climacteric circulatory disturbance.

Hematemesis and Hemoptysis

The same remarks apply to cases of *hematemesis*. Generally, however periodic they may be, they are the manifestation of latent lesions of the stomach, ulcer or cancer.

The periodic *hemoptysis* of the menopause calls for careful and repeated examination of the respiratory apparatus, taking into account not only the present symptoms but the antecedents also. Tuberculous lesions, recent or old, will usually be found. These patches, climacterically congested, may cause a reactivation of arrested foci. Here is such an example.

CASE 9.—E. C., forty-seven years old. During several years of her youth she had suffered from frequent catarrhal attacks, some with fever and profuse expectoration; this made her thin, that is to say, it was almost certainly a tuberculous process which was arrested. Since that time up to the present she had been very well and strong, working hard as a servant, and she frequently boasted of her physical resistance. At her forty-fourth year the climacteric distresses began, being confined almost exclusively

to intense vasomotor reactions—heat flashes; great hypertension tactually, not measured, and abundant metrorrhagias. At the forty-sixth year a considerable hemoptysis coincided with the first missed period. A most careful examination did not permit a diagnosis of any pulmonary lesion. Menstruation then became normal and she felt well for two months. In the following month with another absence of menses, a marked increase of tension again occurred and copious hemoptysis. This time stertor developed with a mild bronchial wheezing and dullness in the right apex; three or four days of fever. Another menstruation the following month, with recurrence of physical signs increasing in intensity and extent in the intramenstrual period, cough, sputum showing Koch's bacilli, and emaciation. The hemorrhages were repeated in the following months and the lesion became outstanding with marked hepatization of the whole upper lobe of the lung; general health bad, making one apprehensive of a galloping course of the process. Later, little by little, the hypertension and the periodic hemorrhages ceased and under strenuous treatment the local and general manifestations improved. Two years later she was much better but the lesions persisted. Definite menopause. A year later aggravation of the pulmonary process and death of patient.

However, in the next case the course was benign:

CASE 10.—S. de P., fifty years old. Suspicious antecedents in her youth—pneumonia twice, repeated catarrhs. No pathologic troubles in maturity. Almost abrupt cessation of menstruation at forty-nine years, with intense circulatory and nervous manifestation. Hypertension—20 maximum; 10 minimum. The first complete absence of the menses was replaced by an abundant hemoptysis. I saw her on the sixth day. Moist stertor, bronchial wheezing and increased râles in the right apex were clearly marked. Very good general state. Opothherapeutic treatment (ovarian) and rest. This episode was repeated in the next month and treatment was intensified. Nothing occurred in the ensuing months. Little by little the physical signs in the apex disappeared and three years later she was very well.

Mammary Hemorrhage

Cases of *vicarious hemorrhage from the breasts* are much more rare. Nostrand, cited by Vinay,³⁰ gives one which is typical. The leakage of blood from both nipples was repeated for several months. Demirdjian³¹ cites another from Cartarz wherein menstruation was abruptly suppressed after a violent emotion, being replaced by a mammary hemorrhage lasting twenty-four hours.

Mammary Hypertrophy and Atrophy

Breast symptoms are rather common in the menopause. In the normal crisis when, as in the majority of cases, characteristic increase in weight occurs, *one of the sites which it elects is the bust*. Sometimes the breasts are increased to an enormous degree. I have seen many women, during this vogue for thinness, who have been annoyed by this development which formerly was considered a sign of beauty. It is certainly very resistant to reducing treatments, as are all localized adiposes. Glandular tissues are not apt to change; nevertheless some cases of true *mammary hypertrophy have been described*. This condition is very rare in the menopause but somewhat more frequent in puberty. Pasquier³² observed two very interesting cases occurring in the later period.

In the more advanced stages of the climacteric submammary fat becomes deposited and the beauty of the bust is destroyed. True *atrophy* of the gland only appears much later, when the senile decline has frankly begun.

Mammary Nervous Upsets

Some women complain of *paresthesias, stinging sensations* and even *pains* in the breast, especially in the nipple, without anatomic lesions being found which would justify these complaints. I have seen two cases of *erotic hyperesthesia localized in the nipple* in menopausal women, who until then had been but slightly excitable sexually. I shall speak of this later.

³⁰Vinay: Op. cit., note (12), page 19.

³¹Demirdjian: Contribution a l'etude de la valeur semiologique des ecoulements sanguins par le mamelon, Thèse de Paris, 1918.

³²Pasquier: L'hypertrophie mammaire de la puberte, Thèse de Nantes, 1921.

Escape of Various Fluids Through the Nipple—Serum, Blood, Milk

Several cases have been published of *abnormal mammary secretions* coincident with the critical age. *The most frequent is the secretion of a serous liquid, thick, at times of a gelatinous consistence*, which exudes, sometimes by expression, sometimes spontaneously, leaving a yellowish stain on the clothing. I have seen five or six such cases.

Exudation of *blood* through the nipple is rarer. When speaking of *vicarious hemorrhages* I indicated the possibility of such discharge appearing monthly from one or both nipples. Again it may not be a true hemorrhage, but the nonperiodic expulsion of *bloody serum* as occurred in the two following cases.

CASE 11.—Woman of fifty-six; observed with Dr. Mendizabel of Renteria. Normal menopause at the forty-sixth year. From then on she presented the phenomenon of expulsion spontaneously or by expression from both nipples of a serous fluid more or less tinged with blood, sometimes rather abundant. She presented no anatomic changes in the mammary glands but the flow was constant and unaccompanied by distress or any local or general symptom. I have not seen her since.

CASE 12.—Woman of forty; unmarried. For a year she had had severe metrorrhagia. Two gynecologists examined her, who made certain there was no anatomic lesion in the uterus or adnexa. Parenchymatous goiter with slight hyperthyroid reaction, fine tremor, tachycardia, nervousness, palpitations. Diagnosis: a premenopausal neurovegetative state. A year later her general health was better; she had increased in weight and the hemorrhages had improved; the hyperthyroidism had vanished. *But from time to time a rather copious quantity of markedly bloody fluid issued from the left nipple, spontaneously or by expression.* None in the other breast. Ovarian opotherapy. Seven months later she was well and the mammary leakage had ceased.

Demirdjian³³ calls attention to the frequency with which these serosanguinous discharges indicate the existence of a mammary neoplasm, especially an intracanalicular or dendritic papillary epithelioma. A cystic fibroadenoma is less frequent and a cystic carcinoma exceptional.

³³Demirdjian: Op. cit., note (31), page 134.

Even rarer are cases of *prolonged lactic secretion after the menopause*. These have been reported in the literature by Altermum³⁴ and Landau.³⁵ To these I may add the following which I saw recently.³⁶

CASE 13.—A woman of thirty-eight; healthy; of asthenic constitution, without salient endocrine changes; multipara, having her last pregnancy without incident three years before. She nursed the child fourteen months normally, but on weaning it noticed that *the lacteal secretion persisted and that the menses did not reappear*. Two years later, when I saw her, the lacteal secretion had not ceased. The milk flowed from her breasts in a fine, short stream on stroking. Microscopic examination showed the lacteal nature of the liquid to be normal but poor in fat. The menses had not reappeared. This woman was, therefore, in the midst of early menopause. She had some climacteric phenomena, chiefly *suffocation*, which still persists. I see her occasionally. Pulmonary findings, pulse, digestive apparatus, etc., normal. Examination of the genital apparatus negative. I gave her ovarian extract for several months, with some interruptions, at the end of which time the lacteal secretion ceased. I saw her two years later in a perfectly normal condition.

It may be assumed that in this woman the hormonal conditions, which facilitate the secretion during the months of lactation and which, in turn, hinder ovarian function, persisted abnormally. Of these conditions the fundamental one must be a *state of postgravid rest in ovarian function*. This is usually transitory, but in this case, doubtless, it was so profound that the activity of the gland was definitely and prematurely annulled while the lacteal power of the mammary organs persisted unduly. Probably other endocrine factors also intervene in the phenomenon of milk secretion—the hypophysis or the thyroid—and perhaps they also collaborated with the ovary in this case. This

³⁴Altermum: Die Folgezustände nach Kastration und die sekundären Geschlechtscharaktere, Beitr. z. Geburtsh. u. Gynäk., 1899, II (Cited by Novak: op. cit., note (17c), page 29.

³⁵Landau: Zur Behandlung von Beschwerden der natürlichen und antizipierten Klimax mit Eierstocksubstanz, Berl. klin. Wchnschr., 1896, xxxvi.

³⁶Marañón: Dos casos de secreción lactea persistente. Revista Medica de Barcelona, No. 1, January, 1924. The other case published in this article refers to a young woman with false pregnancy and prolonged secretion, very interesting but without relation to the climacteric. Therefore I shall not copy it here.

point remains indefinite. The action of ovarian opotherapy is difficult to interpret; to reason, *a priori*, is the resting ovary reactivated and thus the lacteal flow cut short? I doubt whether this is what occurs when the menses do not reappear, for it seems as if they should have reappeared on the awakening of the gland through a therapeutic stimulus. Perhaps, then, the disappearance of the phenomenon was spontaneous.

Mammary Tumors

The menopausal age is propitious for the development of mammary tumors. They are benign or malignant but the former interest us principally. Benign growths were reported by writers of antiquity. Appearing in the critical age, in the form of hard masses in the substance of the gland these tumors are of variable size, that of a filbert, a walnut or even larger. They sometimes occasion complaint because of slight distresses, such as pricks, itchings, stings, or sensations of weight. Again, they appear without any subjective symptom, being then noticed through casual palpation by the woman herself or by the physician.

These benign neoplasms are *lipomas, fibromas, or adenomas*, which while they may later prove malignant, almost always develop favorably, continuing without causing distress for a long time and sometimes disappearing. Besides this, they are differentiated clinically from malignant tumors by their mobility, their clear demarcation from surrounding tissues, their slight sensitiveness to pressure, lack of adherence to the skin, absence of retraction of the nipple, and freedom from metastasis. *When all these conditions are present in a tumor appearing in the critical age, a very careful examination of the lesion will enable us to arrive at a favorable prognosis thus escaping for the moment early surgical intervention.* This last is advisable, as a general rule, in all suspicious tumors of the breast. I have seen various instances of these benign mammary tumors of the menopause which were operated upon early and because there was no reappearance the operations were regarded, without reason, as successful just because of the early intervention. Several cases have also come under my observation in which women refused operation al-

though physicians persistently advised it and the lesion spontaneously disappeared after a time.³⁷

CASE 14.—Such a result is especially notable in the case of an actress who, during the menopausal period, noticed a rather large tumor in the left breast. There were the subjective and objective characteristics of nonmalignancy mentioned above. Various surgeons insistently counseled extirpation of the gland. This she refused because of the difficulties she would experience on the stage in disguising the absence of the breast. The patient was right in this instance, no unfavorable development having occurred during the following six years. It is worth while in this case to point out the *possible etiologic influence of trauma when the actress beat the breasts* in the tragic moments of the rôles she enacted. In other observations this same traumatic influence has been remarked.

Malignant tumors, principally carcinoma, are very frequent in this age. Of these, as of uterine cancers, I may say that their relation to the menopause is purely coincidental. It is a question of the contiguity of the age in which all malignant neoplasms develop. The symptomatology and the treatment of mammary cancer are well known and lie outside this study. Let the physician watch these conditions from the beginning and turn them over at the slightest reasonable suspicion to surgical care.

³⁷Physicians have reproached me for the optimism of my opinion. Some have done so privately and some publicly, like my master Dr. R. del Valle—

Bibliography of the first edition of the *Critical Age*, Revista de medicina y Cirugia practicas, 1919, ii, p. 197. It is clear that in case of doubt it is more prudent to be guided by an excess of caution and to regard as malignant these suspicious tumors of the breast. Yet they rarely, perhaps, constitute a grave element of danger to the patient's life. All in all, as a matter of fact it is necessary to insist on the frequency of benign tumors of the breast and upon the possibility of avoiding useless operations, provided the women be not out-patients, but those who can be subjected to regular medical inspection from time to time.

CHAPTER XII

CIRCULATORY SYMPTOMS

Outline: Circulatory Disturbances and the Climacteric

- (a) Arterial hypertension
- (b) {
 - Dyspnea
 - Factitious urticaria
- (c) {
 - Simple tachycardia
 - Paroxysmal tachycardia
 - Subacute cardiac insufficiency
 - Acute cardiac insufficiency
 - Arrhythmia
 - Anginal phenomena
- (d) {
 - Apoplexy
 - Arteriosclerosis
- (e) Acrocyanosis. Raynaud's disease
- (f) {
 - Varices. Varicose ulcers
 - Phlebitis

Climacteric Arterial Hypertension

Is there a climacteric hypertension? This is the first question we must answer in this chapter. I shall reply in the affirmative, since a careful examination of menopausal women leads me to do so. But the data, furnished by those who have been interested in this period of life and its pathology, are extremely scanty—at times contradictory. The volumes on circulatory pathology scarcely even mention this form of arterial hypertension, a fact doubly strange taking into account its frequency and the pathogenetic suggestions it contains. The problem of hypertension, in spite of all that has been written upon it, is still obscure. Hence I shall give a brief bibliographic review of the question.

Some writers, like Paillard,¹ Kisch,² and Mossacher,³ still con-

¹Paillard: L'hypertension artérielle consécutive à la castration chez la femme. *Le Jour. Méd. français*, 1921, x.

²Kisch: Hypertension und Klimakterium, München. *med. Wehnschr.*, 1922, lxix.

³Cited by Schlesinger: Blutdrucksteigerungen im Klimakterium *Berl. klin. Wehnschr.*, 1921, lviii.

sider climacteric arterial hypertension as infrequent. Paillard, who found cases of high tension in castrated women, states that "only exceptionally" did he find it in the natural menopause. In 253 cases of physiologic menopause Kisch found hypertension in only 61 and in these, with the exception of three, there were causes outside the menopause which explained the phenomenon—such as arteriosclerosis and nephritis. In 39 cases of premature climacteric, normal tension appeared in 19, variable tension in 16, hypertension from nephritis or aortitis in three and in only one was there essential hypertension.

But in general the opinions favoring frequency of climacteric hypertension are more numerous. Of 375 menopausal women Pawinsk⁴ found hypertension in almost all. Meier⁵ found it in one-fourth of his cases. Schickele⁶ and Culbertson⁷ consider the hypertensive phenomenon as fundamental in the circulatory pathology of this age. Hopkins⁸ found it in the 51 cases examined especially for it. Many others agree as to its frequency, among them, Graham Stewart,⁹ Petiteau,¹⁰ Zenope,¹¹ Engelbach,¹² Wilson,¹³ Meyer,¹⁴ Riesman,¹⁵ Gutman,¹⁶ and Schlesinger.¹⁷

As I have said, the general texts scarcely mention the question. Gallavardin,¹⁸ for example, does not mention the climacteric age in his voluminous book on arterial pressure. Oliver,¹⁹ of un-

⁴Pawinsk: Tension artérielle dans la ménopause, Acad. de Méd., 1907.

⁵Meier: Vortrag in der Mittelrhein, Gesellsch. f. Geburtsh. u. Gynäk., zu Frankfurt. December, 1912.

⁶Schickele: Op. cit., note (14), page 19.

⁷Culbertson: Op. cit., note (28), page 21.

⁸Hopkins (A. H.): Climacteric Hypertension: a Study of High Blood Pressure During and Following the Menopause, Am. Jour. Med. Sci., 1919, civ.

⁹Graham Stewart (A): The Prognosis in High Blood Pressure, Practitioner, 1921, cvii.

¹⁰Petiteau: L'instabilité de la pression artérielle minima en période de ménopause, Gaz. hebd. des Scienc. Méd. de Bordeaux, 1924, xlv.

¹¹Zenope: Hypertension artérielle et insuffisance des glandes génitales, Rev. franç. de Gynec. et d'Obst., July, 1922.

¹²Engelbach: La hipertensión asociada con la discrasia endocrina, Jour. Am. Med. Assn., Spanish edition, 1920, ii, p. 22.

¹³Wilson: Cited by Engelbach.

¹⁴Meyer: Cited by Schlesinger: Op. cit., note (3), page 139.

¹⁵Riesman: Hypertensión in Women, Jour. Am. Med. Assn., 1919, lxxiii.

¹⁶Gutman: A Study of High Blood Pressure in Women from the Endocrine Point of View, New York Med. Jour., July, 1921.

¹⁷Schlesinger: Op. cit., note (3), page 139.

¹⁸Gallavardin: La tension artérielle en clinique, Paris, 1920.

¹⁹Oliver: Etudes sur la pression du sang. French edition of the third English edition, Paris, 1922.

doubted authority, declares that "beyond the fortieth year his observations show that the pulse pressure is increased, it being difficult to formulate a rule in regard to this increase * * * nevertheless this crude, but useful rule may be used. To the average pressure before the fortieth year add one for each two years between the fortieth and the sixtieth years and one for each year after the sixtieth." Curiously enough Oliver records this fact of the usual increase in tension after the fortieth year without relating it to the involutional phenomena which occur at this same time.

Kylin's studies²⁰ on arterial pressure constitute one of the most interesting modern contributions to this question. Speaking of the cause of essential hypertension he says "insistence should be made on the well-known fact that the climacteric is frequently linked with this condition. In hypertensions in the male sex, the rise of tension is also seen to coincide with the decline of sexual power, as Munk has noted and I myself have observed. And I have obtained frequently an excellent therapeutic reaction, in certain of these cases, with specific hormonotherapy—testicular extract."

As is seen by this enumeration of foreign data, which does not pretend to be complete, the writers who agree as to the existence of climacteric hypertension are in the majority. It may be stated that those who have investigated the matter have found that the hypertension exists, barring exceptions like Kisch whose findings I cannot explain. Here is the result of my own studies.

The arterial pressure was taken of 106 women who came to our clinic complaining of disturbances related to the menstrual withdrawal which was either beginning or just over. I used the same apparatus, Pachon's oscillometer, with all, at the same hour of the day—five to six o'clock in the afternoon.

From this list there have been eliminated the cases with lesions in the cardiovascular and renal system, which I looked for especially in those presenting greater hypertension.²¹ Nevertheless I am sure that these circulatory and renal disturbances escape

²⁰Kylin: *Klinische und experimentelle Studien über die Hypertoniekrankheiten*, Stockholm, 1923.

²¹This revision brought the exclusion of 292 women who figured in the first edition of this book. There, cases of vascular and renal sclerosis were certainly included. I have excluded these from the new series as far as possible.

the closest examination by present methods. On the other hand I have included the women who presented, aside from the neuro-circulatory symptoms, which we may call "usual" in the critical age, some other pathologic manifestations which are frequent at this period. These are, for the most part, states of climacteric hyperthyroidism, glycosuria and obesity, usually considered as linked with the climacteric.

Relying on my experience, coinciding more or less with that of others, I consider figures abnormal which exceed 17-18 maximum tension and 8-9 minimum tension²² for hypertension, and 12-13 maximum and 6-5 minimum for hypotension. In these 106 cases there were presented:

	CASES	PER CENT
Hypotension	4	3.7
Normal tension	37	35.2
Hypertension	54	51.4
Maximum normal tension and minimum high tension	11	10.4

Therefore, we may say *that coincident with the menopause more than half the women presented a more or less markedly elevated maximum and minimum tension (sometimes of the latter alone) independently of pathologic causes which usually produce hypertension. Hence this elevation should be attributed to the climacteric crisis.*

I have not included men in this table since the critical age occurs later in them, when they present forms of vasomotor sclerosis, which act on tension. Moreover, in the male sex the menopausal phenomenon does not occur which provides a point of reference—a means of defining the limits of the critical period.

Characteristics of Climacteric Hypertension

Here is a detail of practical interest. *In order to appreciate the frequency and intensity of hypertension in climacteric women, it is necessary to make a systematic examination with the sphygmomanometer; since very often the sensation obtained by digital palpation would not make one suspect the existence of hypertension.*

²²The majority of writers consider figures up to 10 (Pachon) as normal. But I make it a rule to examine the arterial pressure in every patient and I consider every figure above 9 abnormal, with the exception of some individuals whom I have not included here.

Moreover, occasionally I have seen women in whom the digital sensation was that of a "weak pulse." There were even other traits inclining one to this diagnosis, yet I was surprised at the high figure observed in the oscillometer. The fact that the hypoplastic arteries concerned have walls which have not yet degenerated and in the obese are frequently buried in fat explains this phenomenon. I dwell on this because of its therapeutic importance.

The intensity of this hypertension is extremely variable. In the 54 hypertensive women, mentioned in the above table, the following figures were obtained.

MAXIMUM	CASES	PER CENT
19	24	44
20	11	22
21	9	16
22	7	12
27	3	5
MINIMUM	CASES	PER CENT
10	40	74
11	8	14
12	5	9
13	0	0
14	1	1.8

I have not succeeded in establishing a relation between these variations and the physiologic or pathologic states in the corresponding women. Greater age does not correspond here to greater hypertension, nor does the intensity of the really climacteric phenomena, nor, I insist on this point, does the presence of some pathologic conditions which are linked to the menopause and which were mentioned farther back. For example, in 15 of these 106 women the hyperthyroid syndrome, so frequent in this age, clearly existed. Yet these cases were divided among the different types of hypertension and normal tension.

According to my observation, which here does not agree with Culbertson's,²³ *the elevation of the minimum tension is rather accentuated, up to the point where, as I said before, it is observed in a group of cases with normal or only discretely high maximum tension.* Naturally it is necessary to eliminate all the pathologic causes which usually give rise to this syndrome of "diastolic hy-

²³Culbertson: Op. cit., note (28), page 21.

pertension" (Gallavardin), such as grave subacute nephritis with early cardiac dilatation, chronic nephritis in the advanced stage, and hypertrophic dilatation of the right cavities with bad venous circulation, advanced vascular cardiopathies, old emphysemas, or severe plethoric obesities.

[According to my earlier observations as noted in my report, the diastolic tension, while elevated, was not increased to correspond with the systolic elevation. Thus the hypertensive patient had a high pulse pressure. Likewise, the diastolic tension was lowered little or not at all in the hypotensive patient, this resulting in a low pulse pressure. Continued observations since have shown these relations to be far from a fixed condition, as the author here indicates. It was rather this extreme instability on the part of the blood pressure and this impaired relation between the systolic and diastolic tensions which I set forth as characteristic, marking it as functional rather than due to organic lesion. This evident variability is emphasized in the following paragraphs.—C. C.]

But, in my opinion, the fundamental character of climacteric hypertension is its variability, its instability. Thus while the hypertension of arteriosclerotics or of chronic nephritics is lightly variable within certain limits, that of women in this age is eminently changeable. It is apt to be accentuated in the menstrual days. It varies from moment to moment during the day, through the influence of diverse factors, like those of digestion, muscular work and above all, the emotions.

Various writers, particularly Oliver,²⁴ have insisted on the fact that frequently the tension obtained in a patient is not the usual tension. It is rather a higher one, influenced by the emotional state of the patient during the process of determining these data. I agree with this and insist that the general practitioner should examine the tension in a systematic way in every patient. Figures should not be accepted until after a second determination, when the patient is calm. If possible the second test should be made at another time—as on the next day. According to my

²⁴Oliver: Op. cit., note (19), page 140.

observation²⁵ it is precisely in these women with climacteric hypertension that this phenomena is found with greater frequency and intensity. That is, tension is increased during the examination through emotion. In exceptional cases this increase may reach 70 mm. But the next day much lower figures will be obtained coincident with patient's state of greater tranquility.

As Schlesinger hints (*loc. cit.*) the divergent results given by different writers is doubtless due, in great part, to this instability of pressure in climacteric women. High figures, normal or even low within certain limits, are obtained depending on whether the determination is made at one time or another. Consequently I insist that the greatest possible number of tests should be made under different conditions, especially from the nervous point of view.

Chronology of Climacteric Hypertension

My data relating to the chronology of this hypertension are scanty, since the collection of figures on arterial tension is difficult and requires much careful, methodical observation in a series of women from maturity to old age. But by comparing isolated observations and those I have made in a series of women I have the impression that climacteric hypertension begins some time before the menopause, in the midst of the preclimacteric period. This should be expected *a priori*, in view of my concept of the involutional crisis. It increases progressively and reaches its maximum coincident with the period of greater turbulence in the general symptomatology. Finally it diminishes, returning to normal, yet generally higher than that of youth. Or else it continues, extending into senile hypertension which is due to arterial lesions produced during the years of the crisis. Here are some observations.

(A) *Cases of climacteric with progressive lowering of arterial pressure.*

CASE 15.—Forty-eight years old. Climacteric hyperthyroidism. Tension, 20-9. Treatment, ovarian extract, antithyroid serum. Twelve months later, tension 16-8; much improved.

²⁵Marañón: Sobre el error emocional en la determinación de la presión arterial. Medicina Ibérica, 1924.

CASE 16.—Forty-five years old. Climacteric hyperthyroidism. Tension, 21-9. Treatment, ovarian extract, antithyroid serum. Ten months later, tension 15-9; much improved.

CASE 17.—Forty-five years old. Climacteric oppressions. Tension, 20-10. Treatment, ovarian extract and belladonna. Twelve months later, tension 16-8; much improved.

CASE 18.—Forty-five years old. Climacteric, neurosis. Tension, 21-12; treatment, ovarian extract, belladonna. Eight months later, tension 19-12; much improvement. Two months later, tension 17-12; improved. Twenty-four months later, tension 23-10; worse. Two months later, tension 20-8; better.

CASE 19.—Fifty years old. Climacteric, asthma. Tension, 21-10; treatment, ovarian extract, iodide of caffenin. Twelve months later, tension 19-9; much improved. Two months later, had stopped treatment, is worse; tension 31-8.

CASE 20.—Forty-eight years old. Climacteric hyperthyroidism. Tension, 23-8; treatment, ovarian extract, serum. Twenty-four months later, tension 20-8; much improved.

CASE 21.—Forty-three years old. Climacteric, ovaritis. Tension, 19-10; local and ovarian extract treatment. Ten months later, tension 15-9; much improved.

(B) *Cases of climacteric with progressive increase of arterial tension.*

CASE 22.—Fifty-two years old. Climacteric, neurosis. Tension, 18-10; treatment, ovarian extract, belladonna, camphor. Fourteen months later, tension 21-10; is worse.

CASE 23.—Forty-eight years old. Climacteric, hemicrania. Tension, 15-8; treatment, diet, ovarian extract, iodine. Twenty-eight months later, tension 20-8; is worse. Great increase in the second aortic tone.

CASE 24.—Forty-seven. Climacteric, hyperthyroidism. Tension, 15-9; treatment, rest in bed, quinine, ovarian extract. Twelve months later, tension 17-8; *is much improved.*

CASE 25.—Forty-six. Climacteric, impaired digestion. Tension, 16-8. Ten months later, 19-8; *is much improved.*

I could cite several more such cases, analogous to these which I have abridged here. *Notice in these the perfect correspondence which almost always appears between the oscillations in the tension and the clinical state*, with the exception of Cases 24 and 25.

Pathogenesis of Climacteric Hypertension

Here we reopen the whole problem of the pathogenesis of arterial hypertension, discussed so much at present, as well as another problem, now in white-heat controversy, that of the intervention and influence of the endocrine factors. I shall attempt to give an outline of both aspects of the question.

Clinicians unanimously admit two types of arterial tension; one, linked with lesions of the vascular or renal apparatus, which is accompanied by the symptoms of these lesions and evolves more or less slowly but subordinate to their well-known course of development. Another is found in cases in which the hypertension is the only phenomenon, frequently unaccompanied by subjective symptoms and in which the most careful examination cannot disclose lesions in the vascular or renal apparatus. This is the so-called essential or benign hypertension.

The hypertensions of the first group undoubtedly depend on the vasculorenal lesion, although the mechanism of this dependence is not yet well understood, and really does not concern us just now. The great question which is still unsolved relates to the origin of the "essential" hypertensions. Do they really appear without any vasculorenal lesion, or are they, too, due to some such lesion which is yet so mild that it cannot be demonstrated by our usual methods? Among recent writers Volhard²⁶ has sustained this latter opinion with the greatest energy. He and his followers believe that this "essential" hypertension corresponds to a latent and lengthy presclerotic period in the renal vessels. Many others, like Monakow²⁷ and Munk²⁸ on the contrary, think that there are cases, confirmed by careful autopsies, wherein hypertension coincides with sound kidneys, both in the

²⁶Volhard. See a resumé of his work in the Monograph *Enfermedades del riñón*, in the *Tratado de Medicina* by Mohr y Staehelin, vol. xii and xiii; Edic. esp. de Calleja, Madrid, 1922.

²⁷Monakow: *Blutdrucksteigerung und Niere*. *Deutsch. Arch. f. kl. Med.*, 1920. cxxiii.

²⁸Munk: *Pathologie und Klinik der Nephrosen, Nephritiden und Schrumpfnieren*, Berlin, 1915.

parenchyma and in the vascular system. Further, they hold that grave renal changes are not accompanied by hypertension, wherefore they assume that this symptom may on occasion depend on other nonvasculorenal lesions or is a strictly functional manifestation, essential, independent of any lesion.

My observations, which are merely clinical, but very carefully collected, coincide with Volhard's in confirming the existence of a *certain number* of "essential" hypertension, without other symptom than the hypertension and in which all tests for renal insufficiency are negative. Yet after a few years minor vasculorenal symptoms begin to appear and finally the typical syndrome of true renal sclerosis is complete. The argument, advanced by Monakow and his followers, that these unquestioned vascular lesions which reach the clinician late are secondary to the hypertension is not convincing, *a priori*. Moreover, the argument is contrary to histologic findings, as those of Volhard, which were so important. He found the vascular change is localized "with extraordinary preference" in the renal vessels. There is no reason why it should not occur in the whole vascular system, if the hypertension were really its cause. I prefer to believe that *our present methods for determining renal function are still crude and do not bring out the earliest pathologic changes, whose only manifestation is this hypertension which is diagnosed as "functional" or "essential."*

Still there are those who hold that, in a *small group of cases*, the hypertension is purely functional, *since it disappears without there being any reason to assume that the supposed cause—the vasculorenal lesion—has disappeared*. Kylin²⁹ brings a great amount of data and argument to support this point, agreeing with me,³⁰ as I remarked before (page 56). In these cases, let me repeat, hypertension is transitory. *It is subject to great daily variations, especially through psychic influences, and is frequently accompanied by diminution of carbohydrate tolerance, hyperglycemia and even transitory glycosuria*. Such conditions are not found in the hypertension of vasculorenal sclerosis, wherein the figures vary little. They remain high and even increase progres-

²⁹Kylin: Op. cit., note (20), page 141.

³⁰Marañón: Ueber Hypertonie und Zuckerkrankheit. Zentral. f. inn. Med., 1922.

sively in spite of treatment, and are not accompanied by hyperglycemia. Kylin adds another difference which he considers essential, but with which I have had no experience, *the state of the capillaries*. These are normal in essential hypertension and, therefore, there is no increase of capillary pressure. In vasculorenal hypertension they are changed and there is an increase of capillary pressure.

Now *the purest cases of this "essential" hypertension are found, as Kylin also recognizes, in climacteric women*. We have already seen that in some cases the hypertension persists and after this period is continuous with senile hypertension. But in other cases the hypertension lessens as the sexual crisis passes, in spite of the fact that the age is then more propitious to the hypertensive state.

How can this essential hypertension of the climacteric be explained? Putting aside the possible existence of incipient vasculorenal lesions in extreme cases, there are those who think that the same pathogenic factors which give rise to the menopausal symptomatology are those which elevate the arterial tone.

The secretions of the different glands which contribute to the climacteric crisis act more or less constantly on arterial pressure.³¹ Thus Culbertson³² has assumed that the *hypophyseal* gland might intervene in the mechanism of this hypertension. Gutman³³ felt similarly in regard to the *thyroid*, and Hopkins³⁴ and Zenope³⁵ suggested the ovary and suprarenals. The intervention of the first two—the hypophysis and the thyroid—is without any physiologic basis. The intervention of the *ovary* is more likely, since this gland seems to have a hypotensive action. The gland's failure, then, would predispose to hypertension, as the following believe: Vincent and Sheen,³⁶ Busquet and Pachon,³⁷ Patta³⁸ and Hare.³⁹ But today we know how presumptuous it is

³¹See as similar articles, Parisot: *Pression arterielle et glandes à secretion interne*. Paris, 1908. Englebach: *Op. cit.*, note (12), page 140. The monographs on each gland in its relation to arterial tension are innumerable.

³²Culbertson: *Op. cit.*, note (28), page 21.

³³Gutman: *Op. cit.*, note (16), page 140.

³⁴Hopkins: *Op. cit.*, note (8), page 140.

³⁵Zenope: *Op. cit.*, note (11), page 140.

³⁶Sch. Vincent and Sheen: *The Effects of Intravascular Injection of Extracts of Animal Tissues*, *Jour. Physiol.*, 1903, xxix.

³⁷Busquet and Pachon: *Choline et ovaire*, *Compt. Rend. de la Soc. de Biol.*, 1910, lxxviii.

³⁸Patta: *Contributio critico allo studio dell'azione degli estratti di organi sulla funzione circolatoria*, *Arch. di Farmacologia*, 1907, vi.

³⁹Hare: *Am. Jour. Obst.*, 1912, cit. by Culbertson, note (28), page 21.

to give a physiologic interpretation to this action of organic extracts on arterial pressure.

This does not apply to *adrenalin*, however. The hypertensive action of this is so clear, so constant, that inevitably one thinks it may be a factor in climacteric hypertension, especially if we take into account the idea that very likely the suprarenals function excessively during the menopause, producing a surplus of adrenalin. This latter possibility was discussed on page 54. There was explained my conclusion that while it cannot be said "that the supposed hyperadrenalinemia of the climacteric may be the cause of the hypertension and the diabetic tendency proper to this age," on the other hand, it is very likely that "it may have an influence, by exquisitely sensitizing the vegetative system, on the production of these manifestations and on the peculiar characteristics which they adopt in this phase of life."

Indeed, the majority of writers, like Volhard,⁴⁰ Kylin,⁴¹ Goldscheider⁴² and Monakow,⁴³ explain arterial hypertension even in cases with vasculorenal lesions, as a state of angiospasm of vegetative-nervous mechanism, favored by hypertrophy of the arterial muscular coat, which occurs after a period of hypertension. Volhard compares this phenomenon with that of asthma, which is also produced through an excitation of the vegetative system whose stimulus may reside either in a lesion or in a nervous excitation favored by humoral conditions, that is to say, the same as in hypertension. Now the hyperadrenalinemia would act, more or less intermittently, "sensitizing" the sympathetic endings in the vessels and also facilitating the action of all the hypertensive factors which, doubtless, are neither so few nor so simple as we imagine.

In summary we may say that *the climacteric hypertension is, in a group of cases, independent of any vasculorenal lesion and then must be attributed to a state of vegetative hypertonia. This latter is probably conditioned by the humoral factors which characterize this crisis, and particularly by the hyperadrenalinemia which is likely to be produced in such cases.* At least, this hypothesis ex-

⁴⁰Volhard: Op. cit., note (26), page 147.

⁴¹Kylin: Op. cit., note (20), page 141.

⁴²Goldscheider: Die essentielle Hypertonie und ihre Behandlung Ztschr. f. physiol. u. diätet. Therap., 1921, xxv.

⁴³Monakow: Op. cit., note (27), page 147.

plains the characteristics and the course of menopausal hypertension very well. I shall cling to it while no better offers.

We must not overlook the fact that there are other pathologic causes, not infrequent in this age, which may act on the hypertensive state of the circulation. Other than initial states of renal sclerosis or general arteriosclerosis already commented upon, these causes are such conditions as plethora in climacteric women with very obese abdomens, or the existence of large fibromas. (Heitz.⁴⁴)

[The relation between fibroid disease of the uterus and hypertension was studied by Polak and his associates, Mittell and McGrath,⁴⁵ in a large number of cases, the study extending over a long period of years. They were forced to the conclusion that there is no effect on blood pressure which can be attributed to the presence of fibroid tumors. In those cases in which hypertension existed coincident with uterine fibroids, the patients were over forty years old, or near the time of the climacteric, or were subject to renal or cardiovascular disease.—C. C.]

Symptoms of Climacteric Hypertension

Let us now consider the clinical consequences of hypertension. *Many women, as I have proved, experience no subjective symptomatology with this hypertension. In others hemicrania coincides with it, or nausea, subjective sensation of palpitation, especially distressing at night, ear noises, or other symptoms which in general are presented in hypertensive states. That the hypertension should pass unheeded in some cases and not in others is probably due to certain conditions of adaptability on the part of the neurocirculatory system—as occurs in the hypertension of arteriosclerosis, and of other organic lesions, which sometimes has a rich symptomatology and again does not give rise to the slightest symptom.*

Vasomotor Phenomena. Suffocation. Symptomatology

The most interesting circulatory symptom of the menopause is *suffocation*, because of its frequency and because it is so typical.

⁴⁴Heitz: Hypertension et fibromes utérines. Bull. de l'Acad. de Médecine, April, 1922.

⁴⁵Polak, J. O., Mittell, E. A., and McGrath, A. B.: Am. Jour. Obst. and Gynec., 1922, iv, 227.

We take it up just after hypertension to profit by some of the pathologic and physiologic data which were explained there and which bear on its pathogenesis.

Here is the symptomatology of *suffocation*. The woman suddenly experiences a *sensation of heat, more or less violent, which sweeps like a wave over her body to her head*. This may come spontaneously or be provoked by various causes such as emotions or digestion. Along with the subjective sensation of heat there occurs an *intense flushing of the face*. Sometimes the symptomatology is limited to this. But frequently after this sensation of heat and erethism *another phase follows, one of depression*. This is accompanied by pallor and profuse sweating, especially on the head, so copious that at times drops run from the skin. Finally, she may have a *cold or shivering sensation* which is more or less violent and lasting.⁴⁶ In some cases, the suffocation is preceded by diverse sensations, true "auras" which the woman recognizes easily. These may be little shiverings, itching sensations or oppressions.

Less frequently these sensations are accompanied or are replaced by severer sensations, such as oppression, anguish, formication, numbness of the extremities, asthenia or even nausea, vomiting or a tendency to syncope.

Generally the suffocations are well tolerated. But in other cases *the intensity of this phenomenon becomes a veritable torment*. I have seen two such cases in which the woman carried her fan to bed. Another patient went to bed whenever the heat flushes occurred. She had to put her hands and face in cool water. In another the sweat was so copious that the patient always kept towels at hand. These were soaked at each attack, especially at night.

[Profuse sweating is an extremely common manifestation in the "suffocation" as experienced in this country. Many times it is present when flushes of heat are not particularly annoying.

⁴⁶"Now she was smothering, flushed, suffocated, covered with sweat. Presently she grew pale, and swathed in her cloak she shivered. Her teeth chattered." Perez de Avala: *Los trabajos de Urbano y Simona*, Madrid, 1923. In this novel are two descriptions of the climacteric—Micaela and Maria Egiptiaca—of admirable exactitude. I shall refer to them again.

I have known several patients who have feared the onset of tuberculosis because of these profuse and drenching "night sweats."—C. C.]

The *number and the duration* of the suffocations are extremely variable. Some women have only two or three attacks a day. Others have them every three hours, or every two, each hour or even more frequently. I have seen examples of all these types. As for the duration, in some cases the phenomenon is fleeting, lasting only a few seconds. [Hence in the U. S. they are often called "flashes." Patients are annoyed by these because they feel that they are blushing although they may not be.—C. C.] In others it continues two or three minutes or more. Cases have been reported wherein the attack was prolonged fifteen or thirty minutes. This time evidently includes the period of the cold and sweaty sensation.

Duration of Suffocations

The suffocations usually begin with the first menstrual disturbances or before them. But they are not apt to reach their maximum intensity until the latter part of the climacteric. *Not infrequently it is the symptom, of all those proper to this age, which endures the longest.* Here are some examples of these prolonged suffocations.

CASE 26.—D. L.—Fifty years old. Sudden menopause at the forty-fifth year. *From then on she suffered suffocations of increasing severity*, accompanied by formication, heat flushes and anguish. The attacks lasted two or three minutes. Arterial tension 18-6; slight diastolic murmur; mild, compensated aortic insufficiency.

CASE 27.—S. P.—Forty-eight years old. Menopause began seven years ago; menses ceased three years ago. *Nevertheless the suffocations persisted with increasing intensity* accompanied by extreme sweating. Arterial tension, 15-8.

CASE 28.—S. C.—Fifty-one years old. Severe hemorrhages at the forth-fifth year were treated with x-ray. The menses then disappeared definitely. *Although six years have elapsed the suffocations continue with great intensity and frequency every three hours.* Tension, 18-11.

When discussing the suffocations of surgical menopause I shall cite cases where the phenomenon was even more lasting.

Pathogeny of Suffocation

Schickele⁴⁷ and Culbertson especially⁴⁸ attribute these vasomotor disturbances to hypertension. They base this assumption upon the fact that these manifestations are presented with the hypertension. In the latter state the manifestations can be produced in men or women by the injection of adrenalin. Let us examine this hypothesis carefully. *In my opinion while hypertension may, indeed, accompany suffocation, and the other vasomotor symptoms, and even take part in their pathogeny, the relation is not one of cause and effect* as the authors mentioned maintain. A consideration of the following facts will suffice to justify the rejection of this supposition. Some of these facts are admitted by Schickele himself. 1. Hypertension which is due to other cause (circulatory or renal lesions) does not produce suffocation. 2. The intensity of hypertension in the climacteric woman is not parallel to the intensity of the vasomotor phenomenon. (Schickele.) That is to say, violent heat flushes and sweating may be presented with but slight hypertension. Inversely, there are extreme hypertensions without vasomotor symptoms. 3. I have been able to prove in a considerable number of women that in the advanced period of the menopause the suffocation has disappeared while hypertension persists. 4. Hypertension is perhaps more intense and constant in the man, during the climacteric, yet suffocations are exceptional. 5. Injection of adrenalin always produces increase of arterial tension but not always vasomotor disturbances (Schickele, myself).

Apart from these facts, by what theoretic reasoning could hypertension become the cause of a vasomotor disturbance, which consists of the sudden vasodilatation of the peripheral capillaries, following their contraction and a compensatory elimination of sweat? [It was the rather marked and frequent rising and falling of the tension while elevated, its instability, which I believed to be the cause of the hot flushes, rather than the mere fact of

⁴⁷Schickele: Op. cit., note (14), page 19.

⁴⁸Culbertson: Op. cit., note (28), page 21.

hypertension itself. Added to this was the observation that suffocations are so often absent in the hypotensive type of climacteric patient. The following paragraph develops this point in greater detail.—C. C.]

The cause of the disturbance in question, is not the hypertension but a vasomotor instability, and note how that word "instability" is repeated to explain each climacteric symptom. This vasomotor instability is produced, as I believe, by an instability of the vegetative system, principally in its splanchnic region (Zondek⁴⁹ and Lapham⁵⁰). And this splanchnic instability is, in its turn, conditioned by the endocrine upsets which characterize the climacteric crisis.

In the present state of our knowledge it is very difficult to explain how these various secretions operate, giving rise to the suffocations. Indeed we do not completely understand the mechanics of the vasomotor innervation,⁵¹ nor of the influence of the internal secretions on this innervation. We stand upon a ground which moves beneath us. All that can be said is, the vessels receive a twofold, antagonistic innervation, vasoconstrictor and vasodilator. We can say that this innervation is furnished through the vegetative nervous system in its two sectors, sympathetic and parasympathetic; and the internal secretions which intervene fundamentally in the climacteric crisis, those from the ovary, suprarenals and thyroid, exert a certain action, although not necessarily on these nervous systems. Let us examine the possible action of the three glands mentioned.

In the first place, *the absence of the internal secretion of the ovary is the initial endocrine phenomenon*, as suffocation is an exclusive symptom of hypo-oöphorism. Increase of the vasomotor reactions has been produced experimentally by type doses of nicotine in oöphorectomized dogs. (Hoskins and Wheelon⁵².) Also, it is in castration that suffocation reaches its maximum

⁴⁹Zondek, B.: Vasomotorische Störungen im Klimakterium, Ztschr. f. Geburtsh. u. Gynäk., 1921, lxxxlii.

⁵⁰Lapham: The Adrenalin Content of the Blood and Its Relation to Vasomotor Instability, Med. Woman's Jour., December, 1922.

⁵¹See the interesting suggestions along this line in: (a) Bard, L.: Du rôle et du mécanisme des actions d'arrêt, etc. Revue Neurologique, 1922, No. 2; and (b) Schrap: Du mécanisme antagoniste des nerfs vasomoteurs, etc. Presse. Méd., 1924, No. 57.

⁵²Hoskins and Wheelon: Ovarian Extirpation and Vasomotor Instability. Am. Jour. Physiol., 1915, xxxv.

intensity. But one interesting fact shows that it is not the absence of the ovarian hormones alone which causes the phenomenon. For that to be true its maximum intensity should correspond to the days which follow removal of the ovary. *Yet clinical experience reveals that suffocations after castration appear after some days of latency. Sometimes, as I have demonstrated, if the one castrated is young, the suffocations are not observed, at least not in their maximum degree until the age of physiologic menopause.* Then, in every case, they reappear with an intensity not apparent since the operation. No doubt during this interval organic reactions have developed in the individual which collaborate intensely in the pathogeny of the symptom.

What are these organic reactions? In my opinion they are the suprarenal and the thyroid hyperfunction. If we admit the existence of a hypersuprarenal reaction in the critical age, and therefore hyperadrenalinemia, as described in the preceding pages, it appears logical to relate the suffocation to the hyperadrenal hypertension. But adrenalin does not give rise to permanent hypertension. As I have said, *we sometimes find women with severe suffocations and little or no hypertension—some even with frankly hypotensive states, as in the following examples.*

CASE 29.—S. G.—Forty-six years old. Two children before her twenty-first year. Then she was left a widow. *Menopause at the forty-fourth year with extreme suffocations, which still persist. Arterial tension 13-9.*

CASE 30.—S. R.—Fifty-six years old. At the fifty-first year metrorrhagias which required the application of x-rays. Menopause. This is one of my cases of greater suffocations—*every twenty minutes, with profuse sweat and nausea—although the tension is only 15-9.*

CASE 31.—M. T.—Fifty-four years old. Married. No children. Menopause due to x-ray treatment for metrorrhagia one year ago. *Since then frequent extreme suffocations with great subjective distress. But the tension is always normal, 15-8, 14-8.*

Of course, the objection can be made that these were cases of permanent hypotension or normal tension *with attacks of hyper-*

tension corresponding to the suffocation. Not long since, Vaquez⁵³ dwelt on this type of error in epilepsy or eclampsia wherein changes in arterial tension occur during the attack which do not give us an idea of the usual tension. In order to settle this point, I have attempted to determine the tension in some of these cases, between the attacks and during them, but have not been able to do so.

Moreover, let me repeat, the adrenalin gives rise, as a more constant and well-known effect to a hypertension through vasoconstriction of the peripheral arteries. But such hypertension is fleeting and this is exactly one of the reasons which leads us to consider adrenalin as the possible factor in the climacteric hypertension which is an oscillatory, inconstant one. Also, adrenalin may give rise to the contrary effect, that is, to vasodilatation and hypotension, either because the doses are small, or as Pende⁵⁴ indicates, through relapse in subjects with a certain predisposition.

In the first edition of this book I suggested that sometimes *this predisposition might be related to the hyperthyroidism which we know is so frequent in this age.* The fact is that the suffocations occur with peculiar intensity in those climacteric women who present hyperthyroid symptoms. Again, there is a certain analogy between the symptomatology of the suffocation and the sensations of heat with perspiration which patients with hyperthyroidism present. Some of these occasionally have to fan or put the hands and face in cold water just as in menopausal suffocations. Finally, and I would stress this,⁵⁵ it is in these patients with hyperthyroidism that an experimental injection of adrenalin, even in small doses, gives rise to a more intense reaction, including among its vasomotor manifestations some which suggest those of suffocation.

However, *these facts are offered only as mere suggestions which are directed uncertainly and hesitatingly toward the target.* Our only definite conclusion is that which we have pointed out before, namely, *the suffocation is due to a disequilibrium of the vegetative nervous system, to an accessional vasomotor instability, caused by*

⁵³Vaquez: Descensos accidentales de la hipertension permanente. Acad. Med. Paris, March 4 and 11, 1919. Ref. in Revista de Med. y Cirug. practicas, Madrid, 1919, ii.

⁵⁴Pende: Op. cit., note (17), page 19.

⁵⁵Marañón: Op. cit., note (1e), page 88.

*the disappearance of the internal secretion of the ovary, sometimes in collaboration with hyperfunctional reactions of the suprarenal glands and of the thyroid.*⁵⁶

I would add two notes to the above before closing. One is the possibility that *the uterus, possessed of an internal secretion as claimed by some, takes part in the production of the suffocation.* This appears to be inferred from Graves' experiments,⁵⁷ according to which, if the uterus be conserved the suffocations do not appear, or are easily tolerated, although the ovaries are extirpated. On the contrary, the conservation or transplantation of a portion of ovarian tissue is useless if the uterus has been removed. But my experience does not agree with this. In a large number of my clinical histories the suffocations were especially intense in those women in whom menopause was effected through radiation of the ovaries. In these the uterus is conserved, probably in its integrity. [Efforts on the part of C. C. Norris and others to show that the uterine mucosa possesses a hormone in its stage of premenstrual activation have not been substantiated by the American or the German writers, but that there is some sort of functional relation between the uterus and the ovaries suggesting a hormonal interaction has some valid support. However, the idea seems to be general that x-ray (or radium emanations) affect the uterus as well as the ovaries, producing an effect much the same as a temporary panhysterectomy would. Hence there would be no uterine influence after raying if ovarian function is suspended.—C. C.]

The other observation to which I referred is this: *the state of the circulatory apparatus probably acts on the intensity and dura-*

⁵⁶Here is the explanation of suffocation which Zondek offers—and Lapham accepts. The sudden contraction in the splanchnic drives its blood content upward, producing the first phase of the symptom, circulatory fullness in the head, with congestive sensation, flushing, etc. After this spasm there follows a relaxation of the splanchnic vessels permitting the return of this blood which had been projected to the head. Then occurs the second phase of the suffocation, that is to say, the debility, almost collapse, with pallor, sweat, etc. Writers explain this sudden vasoconstriction of the splanchnic region by a discharge of adrenalin. But at once this objection springs up. Why are there no suffocations in other states in which it may be assumed there are also sudden discharges of this same internal secretion? Or is adrenalin only thus released in ovarian insufficiency? Accepting, then, the action of adrenalin, some further factor must be admitted in the explanation of the suffocation.

⁵⁷(a) Graves: Transplantation and Retention of Ovarian Tissue after Hysterectomy, Surg., Gynec. and Obst., Chicago, 1917, xxv. See also the articles by E. Ramirez, in this same direction, summed up in, (b) The Endocrine Survey, 1924, ii.

tion of the suffocations. In Case 26 where the suffocations were both grave and persistent, the patient was a sufferer from aortic insufficiency. In general, my clinical impression is that when sclerotic modifications of the arterial system begin, the suffocations reach their maximum intensity. When we come to consider surgical menopause, I shall return to this point.

Vasomotor Instability, Pathogenic Element Common to Emotion and to the Climacteric

Let me note the following suggestion also. It has been demonstrated that vasomotor instability, due to an irritability of the vegetative nervous system and to a complex endocrine disturbance—thyroid and suprarenal principally—plays an important rôle in climacteric symptomatology. Now this same type of mechanism—neurovegetative instability, thyrosuprarenal hormonal disequilibrium—is that which enters into play in the genesis of emotion, as we saw in an earlier chapter. Thus, practically, emotionalism and climacteric are two coincident phenomena. Lange,⁵⁸ with an excellent but incomplete view of the question, localized the mechanism of organic emotion in a vasomotor interplay, the pathologic basis of which is now rather well understood.

Flushing of the Skin. Factitious Urticaria

The vasomotor instability of the menopause frequently causes another symptom—*flushing of the skin*. This occurs spontaneously, or through the force of emotion. More or less irregular and extensive spots appear on the skin, principally on the anterior surface of the thorax and neck. The spots are more or less bright red in color. Sometimes they are prominent, resembling the patches of urticaria—factitious urticaria. These spots are apt to become very marked during examination, as when palpated and because of the patient's emotional state. *In many cases the spots are located exclusively on the thyroid region*, a light pressure sufficing to provoke them. I give much importance to this phenomenon,⁵⁹ as a symptom of slight hyperthyroid reaction which is so frequent in climacteric women.

⁵⁸Lange: Op. cit., note (4), page 89.

⁵⁹See Marañón: La tache rouge thyroïdienne, Soc. Med. des Hôpitaux de Paris, 1922.

Simple Tachycardia

A very constant symptom in the menopause is tachycardia. Writers make a great deal of paroxysmal tachycardia, of which I shall speak presently, but not of simple tachycardia which is permanent, without any subjective sensation and which I believe most frequent. Of 196 women in the various stages of the climacteric, in whom I sought this symptom, I found it in 129. Sometimes it was constant, again it was present only at certain times especially under the influence of exertion and emotional states.⁶⁰ It may be said that while the woman in these years is not subject to tachycardia, in the usual meaning of the term, she at least presents an "instability of pulse" which rises rapidly, on slight cause, from normal to 85, 90, 100 or even higher.

Paroxysmal Tachycardia

Of simple tachycardia the woman makes no complaint. But she does when the tachycardia appears in accessional form and is accompanied by the sensations of violent palpitation, oppression and anxiety which characterize "paroxysmal tachycardia." According to my experience, these attacks may persist for some time after the disappearance of menstruation, they may never cease at all, but sometimes they stop on the conclusion of the crisis. The attack of paroxysmal palpitation is frequently accompanied by the suffocation and vasomotor disturbances just explained. Again digestive disturbances, principally manifestations of flatulence, appear. The attack often comes on during digestion. Other nervous phenomena are present, generally depressive, although occasionally excitant. Kisch⁶¹ gives cases wherein the paroxysm coincided with a voluptuous sensation and ejaculation occurred.

Auscultation almost always shows a considerable increase in the second aortic tone in these cases. I recall one in which I heard a murmur at the apex during the attack, which later dis-

⁶⁰To evaluate these and various other statistics which appear in this book, keep in mind that the material upon which they are based is made up almost exclusively of patients who present a pathologic climacteric. Those who pass through it normally are not apt to be weighed in our balance.

⁶¹Kisch: Op. cit., note (13), page 19.

appeared. Percussion and x-ray did not reveal sensible changes in the cardiac shadow, nor even a noticeable increase in size.

Frequently the subjective sensations which accompany the palpitation are so distressing that they give rise to a deplorable state of mind in the patient. It is sad that nothing, not even the fact that she has been through it before, serves to mitigate the almost mortal terror which is experienced during the disagreeable sensations of the attack.

Pathogeny of Simple Tachycardia.—I believe that *the pathogenic mechanism of simple tachycardia whether permanent or not should be sought in that circulatory instability to which I made reference in the previous pages.* The hyperthyroid factor which so easily explains the tachycardia predominates decidedly in this endocrino-vegetative state. I have already indicated that Bailleur⁶² suspected the intervention of hyperthyroidism in many cases of climacteric tachycardia. *In a great number of these cases I have easily proved other hyperthyroid symptoms*, such as tremor of the hands, retraction of the upper eyelid, slight thyroid hypertrophy and especially loss of weight. In these, consequently, the tachycardia is apt to yield readily to antithyroid treatment.

Pathogeny of Paroxysmal Tachycardia.—Every case of paroxysmal tachycardia presupposes a more or less clear but unquestionable lesion of the circulatory system in its nervous sector or in its system of cardiac conduction. This lesion serves as a *predisposing factor*; that is, it does not give rise to the explosion of the attack. The attack breaks out through the action of another, a *determining factor* which may be an alimentary disturbance, oftenest a flatulent dilatation of the abdomen, an emotion, or a hyperthyroid condition—all very frequent factors in the climacteric and therefore explaining the frequency with which this syndrome appears or is exaggerated during the age of sexual transition. Thus various writers, as Gallavardin⁶³ and Weil,⁶⁴ relate the paroxysmal tachycardia to attacks of hyperthyroidism. I have lately seen various cases wherein typical Basedow's dis-

⁶²Bailleur: Op. cit., note (21), page 20.

⁶³Gallavardin: Nevroses tachycardiques et maladie de Basedow. Arch. des maladies du coeur, 1916.

⁶⁴Weil: Revue de cardiologie de guerre in Les grandes questions médicales d'actualité. Paris, 1918.

ease coincided with the tachycardiac syndrome. Perhaps a sudden secretion of adrenalin plays some rôle in its production, as I indicated in the first edition and as Lapham recently accepted.⁶⁵

Subacute Cardiac Insufficiency

Cardiac insufficiency is a symptom in this stage of life which the practitioner will find interesting. *It presents itself under two forms, slow or sudden.* Slow cardiac insufficiency, subacute, is ordinary hyposystole and occurs in women afflicted with cardiac lesions which are usually compensated. Frequently this compensation may never have been broken during life. For this reason the patient has taken no notice of her lesion, and the first decompensation may be produced by the crisis. According to Kostkebitsh in 25 per cent of these women it is the menopause which is the cause of decompensation. Evidently this may be so since *the sudden and repeated changes in blood pressure and the intense vasomotor reactions of the climacteric place the circulation in such peril that a slightly unstable circulatory equilibrium is easily destroyed.* This instability is greatest when the muscular tissue of the heart and arteries begins to wear out. It is also very likely that *the obesity, which occurs in some women during sexual extinction, may contribute to disturbing the circulatory equilibrium* through the mere size of the annoying mass and, in many cases, through the mechanical difficulty which the accumulation of subdiaphragmatic fat occasions. On the other hand, *I do not believe that the "cardiac adiposity," which is given great importance by Kisch,⁶⁶ and others, in the origin of climacteric disturbances, takes part in all of them.* With Bonilla⁶⁷ I recently studied a fatal case of colossal obesity due to premature ovarian insufficiency. At autopsy I fully confirmed my conviction, which is based on a long series of postmortem observations, that *adipose overburden of the heart* as a factor which would deaden its function is entirely fantastic. In this case the obesity was immense and of such kind that it rendered circulation difficult causing sudden death. Yet the pericardial adiposity was moderate. Like findings are observed in many other autopsies wherein a similar

⁶⁵Lapham: Op. cit., note (50), page 155.

⁶⁶Kisch: Op. cit., note (13), page 19.

⁶⁷Marañón y Bonilla: Op. cit., note (25), page 112.

diagnosis had been made during life.⁶⁸ Not even theoretically can an accumulation of fat be easily conceived sufficiently large to deaden the contraction of the strong cardiac muscle.

Clinically these states are like the usual hyposystolic and asystolic ones and need no description here. I shall only note that *from the prognostic point of view there is hope that circulatory equilibrium will be permanently restored when the menopausal crisis passes and a new normal state is reestablished.* But this does not happen always, unfortunately. My experience inclines me to the opinion that the arterial walls and the cardiac structure having been out of order for a time, react badly when old age begins and do not always achieve the complete compensation of the preclimacteric years. *Let us note the usefulness, from the therapeutic point of view, of combining in these cases opo-therapeutic remedies with proper tonic medication.* I shall discuss this again in a later chapter.

Sudden Cardiac Insufficiency

Sometimes the circulatory insufficiency occurs suddenly, a sudden asystole provoked by a minor cause, such as a walk, indigestion or grief. Texts do not call attention to this symptom, the most serious cases of which I have seen in the menopause. Here are two examples.

CASE 32.—Woman of forty-six years, of poorly developed constitution; hereditary syphilis likely; menses regular. At twenty-nine she had a child; parturition difficult because of a narrow pelvis. At that time a systolic murmur due to mitral insufficiency was found; well compensated. She had no more children and did not present any further phenomena of circulatory decompensation. At forty-three she began to have irregular periods, without any noticeable climacteric symptoms. A year later, one day just after a moderate walk, it tired her a little to climb a small hill opposite her house. That night a *collapse suddenly occurred, with severe cyanosis, imperceptible pulse, and disappearance of the murmur*, according to the physician who at-

⁶⁸Very recently I made an autopsy in another case of colossal obesity, from hypophyseal hemorrhage. Here, too, death was due to cardiac insufficiency, and the precordial, precardiac and myocardiac fat was likewise very moderate. The important factor is always the abdominal fat.

tended her at that time. She reacted poorly to emergency treatment (caffeine, camphor oil, etc.). Anuria and anasarca in the following hours. All these symptoms lasted three days, at the end of which, digitalis, corpus luteum, milk diet and rest succeeded in reestablishing circulatory equilibrium. Four months later during the days when she should have menstruated the asystole recurred with much less intensity. She was very well then for three years, with a little fatigue on effort. The periods had ceased. She died of uremia.

CASE 33.—A woman of fifty; multipara; always well and menses regular. She had no circulatory symptoms and her physician said that auscultation was normal. At her forty-fifth year the periods began to skip and she complained of great suffocation with palpitations. Deep melancholia with attacks of irritability. It was observed that she tired a little more in climbing stairs than before. This was attributed to the fact that she had put on considerable weight. One night, coinciding with a skipped period, she came in from the street very hurriedly, and on lying down had a spell of vomiting and nausea which she attributed to indigestion. She then suffered *a sudden collapse, with severe cyanosis, bloating, very small and irregular pulse and semidelirium*. I saw her in the early hours and found her in a state of grave hyposystole; negative auscultation, except loss of the tones. With suitable treatment (digitalis and corpus luteum) she reacted quickly, except for a malleolar edema which lasted some time. She had no further attacks in spite of climacteric disturbances, principally nervous, very intense and persistent, although always amenable to opotherapy. Careful and repeated auscultation after the attack revealed no murmur; only a general reduction in the tones and a slight accentuation of the second pulmonary sound; at times some intermittency; arterial tension variable, but in general below normal (maximum 12, minimum 7 in one estimation). Cardiac feebleness, with normal percussion. Urine normal. Four years later the patient was well, according to indirect information.

The first case was one of compensated mitral insufficiency. The second was probably one of slow, light myocarditis of unknown origin. In both, data appears which allow one *to suspect*

a syphilitic infection. The circulatory conflict inherent in the crisis gave rise to the sudden asystolic state on the provocation of small exertion which was, however, excessive for the deficient strength of the circulatory situation. This asystole was succeeded, after the disappearance of its cause, by adequate functional re-establishment.

Mechanism and Prognosis of These Seizures

I would insist strongly on the physician's use of judgment in evaluating the part which the menopause plays in these attacks. They always presuppose a lesion, sometimes imperceptible, but certainly present. In an organism with a healthy cardioarterial system, the menopause alone by its intensity can produce circulatory disturbances which are more or less troublesome but mild, such as vasomotor phenomena, tachycardia and palpitation. But it can never cause this sort of grave complication. My experience along this line has been particularly rich since the first edition of this book was published. I shall add no new case reports, since they all teach the same lesson as those given above, which may be considered as typical. The fact that the patient recovers her circulatory equilibrium after the crisis is past does not invalidate my hypothesis of the "constancy of the lesion," as Valle⁶⁹ has hinted. When the "occasional moment" has passed, the lesion may return, indeed, to its "latent form." But one may feel sure that eventually the majority of these patients will die of heart disease.

Arrhythmia and Climacteric

The circulatory manifestation which, perhaps with greater reason, justifies a favorable prognosis because it is a purely functional climacteric disturbance, is arrhythmia. Indeed, rather frequently I have seen women whose histories would not lead one to suspect circulatory lesions, examination being actually negative, yet menstrual disturbance *was accompanied by arrhythmia, either permanent or accessional, with or without subjective disturbances.* But the arrhythmia always disappeared when the postclimacteric

⁶⁹Valle Aldabalde: Op. cit., note (37), page 138.

stage arrived. Again, the arrhythmia coincides with attacks of suffocation. Or it may be presented with paroxysmal tachycardia. Here is an example, one of many such.

CASE 34.—S. de A.—Forty-nine years old. Multipara; no cardiac antecedents. *Coincident with the menopausal disturbances, principally suffocation, severe arrhythmia was presented* without tachycardia, accompanied by subjective distress and great anxiety. For two years she lived a slave to her pulse. Heart and kidneys sound. Electrocardiogram normal. With the cessation of the menses the circulatory disturbances stopped. Three years later she died of mammary cancer.

In the next case the arrhythmia appeared after castration.

CASE 35.—S. de N.—Married; no children; purulent adnexitis; total extirpation at the twenty-ninth year. Since then severe distress from ovarian insufficiency, accentuated at the time I saw her in her forty-fifth year, the period of the physiologic climacteric. The distress was characterized by increase in weight, suffocation and *severe arrhythmia* which greatly exhausted her. No cardiac symptom. Kidneys sound. Arterial tension 19-18. I administered cardiac tonics, ovarian extract, sedatives and psychotherapy. The entire syndrome disappeared and thereupon the arrhythmia also disappeared. Eight years later she is very well.

To sum up these cases: the arrhythmia may be either the first indication of a circulatory decline or a simple functional disturbance without prognostic consequence. But, let me repeat my advice, one should not pronounce this "climacteric" as of good prognosis until after a very extensive and careful examination.

Anginal Phenomena in the Menopause

These reservations must be made especially in certain symptoms of sternalgia, with the complete or incomplete form of angina pectoris. This appears not infrequently in climacteric women. They are usually presented in cases of obesity with hypertension, according to my experience, and improve with hypotensive and reducing treatment. I refrain from considering these symptoms benign because they coincide with the menopause, since they presuppose a painful effort on the part of the heart under a cir-

culatory disequilibrium and we cannot foresee clinically, but can only judge *a posteriori* from the attack, whether that effort will be sufficient to reestablish the equilibrium. In general I have always recommended greater caution in diagnosing as "false" angina pectoris appearing after the fortieth year. For the rest, the symptomatology is the same as that of true anginal attacks. The patient is suddenly seized with a sternal or epigastric pain, with various radiations to the breast and left arm—sometimes these do not appear—with sensations of cardiac oppression or of very distressing thoracic fullness, a pallor occasionally and irregular pulse.

Neurosis and Apprehension Due to Angina Pectoris

Let us not forget, however, that there is an *apprehension of angina pectoris*, among a great many neurotics, of whom a rather high percentage is recruited from climacteric women. The patient interprets the attack as anginal, with imagined or real distress, but there is nothing objective to be seen such as paresthesia, rheumatic pain, or oppression with suffocation. I emphasize the fact that the *neurosis of angina* has no objective distinguishing marks like so-called *false angina*. Physicians see patients of this type almost every day, who are considered anginal for purely fantastic reasons. Let me set down the following case as being very characteristic.

CASE 36.—Sister L. M. Forty-nine years old. Very intelligent and active. Thin, nervous. No special antecedents. For the last two years menstrual disturbances which had now disappeared. A month ago, suddenly, pain appeared in the sternal region, coinciding with a "suffocation," fear of impending death, pallor, feeble pulse, sweating. This greatly alarmed her and the other nuns. Camphor oil was given, the confessor summoned. This attack was repeated at various times. A *diagnosis of angina pectoris was made*, and her physician accepted it. I saw her in consultation, as a very grave case. She was as white as milk, debilitated; had been in bed several weeks. Her heart, arterial tension and kidneys were entirely normal. A rigid investigation as to the painful attacks, their exact coincidence with the suffocations, the exalted atmosphere of the convent, and the discov-

ery that she had witnessed the fatal angina of a relative whom she had nursed allowed me to offer a favorable prognosis. Recovery was achieved through psychotherapy.

Apoplexy

Apoplexy used to have an extraordinary importance in climacteric pathology. As the years for the highest incidence of apoplexy Hippocrates gave "a quadragesimo anno ad sexagesimum." And Gardanne,⁷⁰ whom we quote as a writer of the pre-experimental era, states that "the death of women through apoplexy in the menopause has been proved many times." *But now we are certain that this is a very rare phenomenon and that when it occurs it does so in women with previous deeply seated lesions of the arterial system*, as Windschied has stated and the experience of Recasens and other recent writers confirms.⁷¹ Women troubled by "suffocations" of a certain intensity, suddenly feeling the blood rush to the head, with a sense of oppression, nausea and dizziness believe that apoplexy threatens them because this symptomatology coincides with that presented at times by patients having true apoplexy and because these symptoms are a matter of common observation through their frequency. The physician should know that such a fate does not await every patient presenting these symptoms, and having satisfied himself as to the state of her arteries, he should make every effort to calm her.

Arteriosclerosis and the Critical Age

This leads us to a discussion of the so-called *climacteric arteriosclerosis*. The classic writers frequently mentioned this complication of the menopause. Now we know that the crisis may produce states of essential hypertension, but *when we find arterial lesions in a woman between forty and fifty years of age, we may be sure that they are due to other pathologic causes—not to the menstrual upset alone*. Aside from this, climacteric hypertension, as has been explained, lacks the characteristics of the hypertension of arteriosclerosis. The first is transitory in a consid-

⁷⁰Gardanne: *Avis aux femmes qui entrent dans l'age critique* Paris, 1816.

⁷¹Recasens: *Op. cit.*, note (1), page 101.

erable number of cases, disappearing and giving place to a period of normal tension which either continues until death or is succeeded by the hypertension of senile arterial sclerosis. Again, menopausal functional hypertension is continuous with the hypertension of arteriosclerosis and I need not point out how difficult—how impossible indeed—it will be to diagnose the case properly. Here, as in many other parts of climacteric pathology, that which we may call physiologic (due purely to the crisis) and that which we may call pathologic (produced by lesions coincident with the crisis) are so interlaced that, as stated in Chapter VII, I prefer to study them together. To attempt a separation is futile and the result would be merely artificial.

Let me point out that sometimes this confusion in symptomatology has a pathologic reason which justifies it. Sometimes the same neurohumoral causes, which appear to give rise to the essential hypertension of the menopause, aid fundamentally in producing the arteriosclerotic lesions. We cannot now admit that arteriosclerosis is due to an excess of circulating adrenalin, as Josue claimed twenty years ago.⁷² But neither can we overlook the fact that this supposed hyperadrenalinemia *contributes, with other factors*, to the vascular lesion.

On the other hand, we now know, according to the studies of Chauffard and his collaborators⁷³ that when circulating cholesterol is excessive, it accumulates at points on the intima, with beginning necrosis initiating the first phase of the atheromatous scale which, consequently, is no more than a "local deposit of cholesteroline." Furthermore, the same writer has noted that there is almost always an excessive proportion of this lipid in the blood of arteriosclerotics. I have confirmed this finding, as have many other investigators. *According to all probability, there is a hypercholesterinemia in the climacteric transition* (see page 62) *which is due to the hyperplasia of the suprarenal cortex. This would be another circumstance favorable to the production of arteriosclerosis in this age.*

⁷²Josue: Atherome experimentale par injections repetées d'adrenaline dans les veines. *Compt. Rend. de la Soc. de Biol.*, 1903. See an excellent resumé of the present state of the question in Pende. *Op. cit.*, note (17), page 19.

⁷³See: (a) Chauffard: Les depot locaux de cholesteroline et leurs rapports avec la cholesterinémie. *Rev. de Méd.*, Oct., 1911. (b) Grigaut: *Op. cit.*, note (30), page 62. (c) Guy Laroche: *Op. cit.*, note (31), page 62.

Acrocyanosis. Raynaud's Disease

Contrary to current opinion, which regards these processes as youthful syndromes almost without exception, I have seen a certain number of cases wherein the onset corresponded to the climacteric years. I consider *acrocyanosis* as an attenuated state of *Raynaud's* disease but as a purely functional vasomotor disturbance, whereas in *Raynaud's* disease a lesional element in the arterioles has been added to the nervous element. This has been brought out by Castellino and Cardi,⁷⁴ among others. I have confirmed it in a case of *Raynaud's* gangrene in the nose. This case is recent and as yet unpublished. Although *acrocyanosis* and the first phases of *Raynaud's* disease belong rather to early life, the phenomenon of grave asphyxia and gangrene in the latter disease almost always appear in persons of a certain age or in the young who have premature arterial changes.

As for the vasomotor phenomenon, common to both cases, it is, at least in a great number of cases, related to ovarian insufficiency. I have demonstrated it and precisely because of its relation I give the name "hypogenital hands"⁷⁵ to this cyanosis accompanied by hypoovarian symptoms. Whether in the young or in the mature, ovarian insufficiency is almost always constant in this syndrome. Dalché⁷⁶ agrees with this point of view, for *Raynaud's* disease coincides almost always with amenorrhea. Other writers have recently pointed out the association between this process and lesions of the hypophysis (Pribram⁷⁷) and they have obtained good results through opotherapy, using this gland.

Varices. Varicose Ulcers

The "plethora diathesis" of the critical age favors the appearance, or the aggravation, of varices which are so frequent in women, especially in this age. Their symptomatology is so well known that I need not emphasize it. They appear preferably in the obese and hypertensive multipara.

⁷⁴See Castellino e Pende: Op. cit., note (1), page 73.

⁷⁵See Marañón: Op. cit., (11), page 103.

⁷⁶Dalché: Traitement médical des maladies des femmes, Paris, 1922.

⁷⁷Pribram: Hypophyse und Raynaud'sche Krankheit, München. med. Wehnschr., 1920, No. 45.

The classics speak of the relation between *varicose ulcers* and the critical age. Given the present concept of varicose ulceration we cannot admit this relation exists. I regard them as a trophic disturbance of the skin, in the pathogeny of which the circulatory factor enters and probably also a dysnutritive factor, analogous to what occurs in the production of the cutaneous lesions of pellagra and of the so-called decubitus ulcers of typhoid fevers—in short, elements which have nothing in common with the critical age.

Phlebitis

Painful symptoms and slight swellings are apt to appear in the affected leg in those women who have had *phlebitis* during the period of genital activity. These may be interpreted as an attack of periphlebitis, started by the circulatory and toxic disturbance of the climacteric. They usually yield easily to elementary care, such as, brief rest, nocturnal elevation of the leg, and light massage.

CHAPTER XIII

NERVOUS SYMPTOMS

Outline

- (a) { Nervous symptoms of the climacteric
Neuralgia
Headache
Hypertensive headache, indurative headache
Bone pains, rachialgia
Painful uneasiness of the legs
- (b) Asthenia
- (c) { Paresthesia
Pruritus
- (d) Sensoral disturbances
- (e) Dizziness
- (f) { Insomnia
Somnolence

Neuralgia

In the first place let us consider the *neuralgias*, which render life miserable for many menopausal women.

These neuralgias often affect different nerve regions of the body such as the trigeminal, dental, cervical, intercostal, lumbar and sciatic. They are presented either in the form of attacks coincident to the days of menstruation, or in a continuous or irregular form. Their course is the usual one, without other peculiarity than their coincidence with the climacteric and lessening when this is past. But sometimes they are prolonged indefinitely, proving rebellious to anticlimatectic treatment which is apt to be useful earlier.

Headache

In a considerable number of cases *headache* either appears or is aggravated if it already exists. But more frequently, perhaps, this trouble has coincided throughout life with the men-

strual periods, and *in the menopause after a period of exacerbation it diminishes and finally disappears*. I might cite several histories of women from whom I have heard the oft-repeated phrase, "Since I became old my headaches left me." Lührs recently called attention to this fact¹ and related it to the action which pregnancy also exercises on headache. He attributes it, at least in a group of these cases, to a "dysovarian" etiology and speaks of good clinical results from luteinic and placental opotherapy.

Hypertensive Headaches

I have seen terrific headaches in climacteric women with much hypertension. The headache is sometimes accompanied by vomiting, dizziness, congested facial aspect and finally a general syndrome which may take on an alarming appearance, but which usually disappears without leaving traces when the hypertension lessens. While various writers like Walton, Paul, Thomas or Cabot² speak of hypertensive headaches, none of them and none of the current texts relate this form of headache to that which so commonly affects women in the critical age.

Indurative Headache. Its Relation to the Menopause

In some cases of men and women of this age, I have seen the *indurative* headache which was described some years ago by Edinger.³ This form of headache is characterized by the existence of painful swellings at the cranial points of insertion of the muscles of the neck and of the nape of the neck, involving the trapezius, scalenus, sternocleidomastoid and others. The pain, dependent on these lesions is localized principally in the nape of the neck, although not exclusively, and has no special characteristic. These swellings appear tactually as hard accumulations within the muscle mass. Their size varies from that of a hemp seed to a spot as large as a centime and they are very sensitive to pressure.

According to Edinger, this form of headache is the most frequent of all, as the majority of the cases of so-called *rheumatic*

¹Lührs: *Einwirkung auf Migräne bei Frauen durch Sexualoptone*, Deutsch. med. Wchnschr., February, 1923.

²Cabot: *Diagnosi diferenciali*. Edic. italiana, Milan, 1916.

³Edinger: *Die deutsche Klinik*, 1903.

headache would be included in this type, if carefully diagnosed. It is obvious that this statement is exaggerated, and the fact that Edinger's opinion is scarcely known shows it enjoyed little success in practice. Physicians are always ready to accept new clinical ideas when they lead to a fairly good clinical result, remembering the meagerness of the remedies upon which we must rely in the treatment of headaches in general. Nor can I agree with Cabot⁴ whose broad and careful experience permits him to say that he never encountered a single case which exactly corresponded to Edinger's description of indurative headache. I have seen at least three very marked cases, which, because of the rarity of this affection, I shall describe briefly. The three cases, two women and a man, were in the normal or pathologic critical age.

CASE 37.—Woman of forty-nine years. Always very strong. Rheumatic antecedents. Multipara. Very regular. Now in the menopause which was characterized by intense metrorrhagias, alternating with months of amenorrhea; intense vasomotor phenomena, pharyngeal spasms, general nervous excitation and, especially, poor emotional control and *attacks of intense pain in the nape of the neck*. On careful examination, *several indurated nodules, very sensitive to pressure*, were found in the *occipital insertions*. Massage and hot local applications and ovarian opotherapy gave quick relief. Three years later she was entirely well.

CASE 38.—G. C. Man fifty-nine years old; very rheumatic; always strong; active and prolonged sexual life. In this age he began to suffer from nervous disturbances with tendency to melancholia, digestive disturbance and flatulence and circulatory troubles, chiefly hypertension. These symptoms, together with a marked increase in weight—abdominal especially—I interpreted as the consequence of the masculine climacteric. Finally, he suffered, particularly on the days he worked hard, from *violent attacks of pain which began on both sides of the occipital insertion and at once extended over the whole head*. He had learned by himself to relieve these attacks with hot local applications. On examination I found *the occipital insertions*

⁴Cabot: Op. cit., note (2), page 173.

studded with innumerable painful nodules. The attacks continued for several years and were always relieved by the same treatment.

CASE 39.—S. de E. Thirty-six years old. The menses became intermittent two years before, and a considerable increase in weight had coincided with this, the localized deposits being especially marked in the sites elected in hypogenital obesity; a marked nervous state and *terrific pains in the head*, which began on the left side of the nape of the neck and extended to the whole of that half of the head. *Two or three indurated and sensitive areas* were clearly felt in the insertions of the occipital muscles on both sides. Local treatment by massage and heat and opotherapy, ovarian and hypophyseal extract, gave quick relief. Relapses occurred in two years, when the treatment again relieved her. The menses had disappeared.

Here, then, are three cases which can be diagnosed unquestionably as *indurative headache*, and of the three, in two, there were intense climacteric disturbances and in the third, premature ovarian insufficiency. *Thus a certain relation, at least one of chronologic preference, may be suspected between these changes and genital insufficiency.* This relation has been confirmed through the success of opotherapy in two of them and in others which are less typical and which are therefore not mentioned. Achucarro told me of some similar cases which he had observed.

Bone Pains. Rachialgia

A special interest attaches to the bone pains of which women often complain during the menopause. Writers who have discussed this question describe it in similar words. The pains affect the legs, the arms, and *especially the sacral and lumbar region* and the rest of the vertebral column. The painful areas and the whole backbone are often sensitive to pressure. The persistency of these complaints may bring despair to the patient, rendering her irritable and preventing rest in bed.⁵

⁵"Sometimes she was attacked by unusual forms of pain, which she always expressed as inquisitorial, associating her tortures with those described in a book which she had read in childhood, *Las Mazmorras del Santo Oficio*. 'It is as if I were being broken on the wheel. My bones hurt me, especially my hips. You can hear them crack.'" Perez de Ayala: Op. cit., note (46), page 152.

[Cecil and Archer⁶ have described these "bone pains" as occurring in women during the menopausal years. Their report included fifty cases, the youngest forty-two years of age, the oldest sixty-six. There was no racial predisposition. They regard these pains as due to an arthritis noninfectious in origin, and affecting oftenest the knees, fingers, shoulders, feet, and lumbar spine. There was no periarticular inflammation or thickening demonstrable. They regard this development as a definite clinical syndrome, a chronic polyarthritis of obese middle-aged women characterized by a persistent stiffness and pain in the joints affected and definitely related to endocrine disturbance. It runs a mild chronic course and is treated by the iodides, a low calory diet and the usual physiotherapeutic measures.—C. C.]

Painful Uneasiness of the Legs

Windscheid, cited by Kisch,⁷ gives some cases of women who were *compelled to move their legs constantly* because of these pains in them. I have observed this same phenomenon in six cases. It was so intense and marked that it may be useful to give them here.

CASE 40.—S. de V. Fifty-one years old. Always well. Sudden menopause at the forty-first year coincident with an intense emotion. From then on increase of weight; sensations of cold and various nervous disturbances; but the dominant symptom was a *painful uneasiness in the legs which obliged her to move them ceaselessly*, an action noticeable to those about her.

CASE 41.—S. de L. M. Fifty-three years old. Multipara. Menopause at the forty-eighth year. Since then various complaints, which were difficult to put in proper order through questioning, but which gave rise to a typical and intense form of postmenopausal myxedema. One of the principal manifestations of which the patient complained and which attracted the attention of her family was the *constant uneasiness of her legs*, stubborn, indefinite, and which never left her. This woman was

⁶Cecil, R. L., and Archer, B. A.: Jour. Am. Med. Assn., 1925, lxxxiv, 75.

⁷Kisch: Op. cit., note (13), page 19.

regarded for a long time as a cardiac case because of a hypothyroid goiter. Upon a more accurate diagnosis, she was quickly relieved by thyroovarian therapy. The restlessness in the legs also disappeared. Four years later she died of uremia.

CASE 42.—A man of fifty-five; an actor, with severe arthritis and neuropathic antecedents. For two years he had suffered from intense nervous phenomena, with a tendency to melancholy, intense flatulence, persistent increase in weight, localized fat on the abdomen, and various other climacteric manifestations. One of the symptoms of which he *complained the most was a painful restlessness in both legs, which forced him to move them continuously* whether sitting or standing, and which disturbed his performance on the stage. I know nothing further of this case.

CASE 43.—S. C. Thirty-eight years old. Unmarried. Severe metrorrhagia which required the use of the x-ray two years ago; since then, suffocation, increase of weight, and *marked painful restlessness in the legs*. She could not keep them quiet; this was felt for only short periods of time. She improved under such treatment as diet and ovarian extract.

CASE 44.—F. de B. Forty-two years old, married, multipara. The menses began to fail a year previously and she presented suffocation, increase in weight, and chiefly "*an impatience in the legs*," as she expressed it, which embarrassed her constantly. I did not see her again.

The relation between this phenomenon and genital insufficiency appears very clearly in the following observation of premature climacteric.

CASE 45.—F. G. Thirty years old; married, no children. A year previously her father died suddenly, and at once the menses ceased and various nervous and vasomotor phenomena appeared, chiefly a typical and *marked painful uneasiness in the legs*. I did not see her again.

Pathogenesis of These Painful States

Heretofore these pains were considered as neurasthenic symptoms and, with the depressing manifestation of the nervous system frequently observed in this age, made up the picture referred

to as neurasthenia which then was considered a most frequent complaint in the menopause. Beard said that "if the backbones of all the women on Fifth Avenue, New York, should be carefully examined spinal hyperesthesia and pain in the dorsal spine would be found in almost every case." Now we do not interpret this fact as does this writer, the creator of the concept of neurasthenia. Pineles⁸ regards these data as of a *pseudogouty* nature, that is to say, related to metabolic disturbances, dependent on ovarian hypofunction. Later I shall dwell upon the relations which link gout to genital insufficiency. Schickele,⁹ finally, *establishes a direct relation between the bone pains and the ovarian upset*, and he bases the assumption upon the fact, which I have often verified, of the efficacy of the genital opotherapy in its treatment.

In order to explain *painful uneasiness of the legs* we might think of the frequent hyperthyroidism of the critical age, since it is recognized that motor uneasiness is very characteristic at this time, often recalling this particular symptom. Nevertheless, I ought to say that in the cases given there was not the slightest trace of hyperthyroidism.

[I have noted several cases of this "pedal restlessness" during the climacteric years. One of the most marked was that of a patient showing definite hypofunction of the thyroid and hypophysis. She was small featured, plump and complained of impaired memory, was easily fatigued, could not keep the back of her neck cool and was equally unable to keep her feet warm or quiet when trying to rest. This condition obtained before menstrual suppression but with the skipping periods the pains and uneasiness in her legs became less marked, whereupon lumbosacral backache supervened.—C. C.]

As for the *visceral neuralgias*, such as sternalgia, gastralgia and enteralgia, described in the menopause, I have spoken or shall speak of them in the proper chapters.

Sensation of Asthenia. Its Endocrine Pathogenesis

Very frequently a sensation of asthenia, of fatigue, is very characteristic in the nervous symptomatology of the critical age. It

⁸Pineles: *Pseudo-gicht.*, Wien. klin. Wchnschr., 1908.

⁹Schickele: *Op. cit.*, note (14), page 19.

was also considered as one of the symptoms of climacteric neurasthenia. But it is undeniable that it is presented in many women who are not neurasthenic, appearing sometimes as the sole nervous symptom. Again it is accompanied by states of mental depression or true melancholy.

Formerly asthenia was considered as a special symptom of suprarenal insufficiency. We know now that it is presented not only in this state, but also in many endocrine upsets. It also appears in states of exactly opposite pathogenesis, as in thyroid insufficiency, hyperthyroidism, and in diseases of the hypophysis, although it is in suprarenal insufficiency that it reaches its greatest intensity and frequency. Recently¹⁰ I dwelt upon the caution with which one should regard this symptom from the diagnostic point of view. The fact is that every endocrine change can give rise to this sensation of asthenia, probably because of the disequilibrium which it produces in the vegetative system. Thus it is very difficult to separate purely nervous asthenia and true muscular exhaustion.¹¹ The endocrine complexity of the climacteric explains the frequency with which we encounter the symptom whatever its origin.

Paresthesias

Many women, in the critical age, complain of *various paresthesias, principally sensations like formication or numbness* in the fingers and toes or, less frequently, in other cutaneous regions. Discarding those cases in which these paresthesias are the indication of organic disturbances (as renal) there still remain some which can be interpreted as of a purely vasomotor or nervous origin (see page 152). This manifestation is apt to alarm the patient, as she believes herself afflicted with a grave circulatory process.

Generalized Pruritus. Its Relation to Hyperglycemia

Another very common and very painful symptom belongs clinically to this order of phenomena, *generalized or localized pruritus*.

¹⁰See Marañón: Op. cit., note (11), page 54.

¹¹Recently in a typical and very grave case of Addison's disease, I was able to prove, through ergographic comparisons with other patients, that even in the asthenia of this disease there is also much nervous asthenia.

I have often seen *generalized pruritus* at this age. Sometimes it is so rebellious to treatment that it seriously hampers the patient's life. Considering the frequency of diabetes at this age, sugar in the urine is the first thing to be looked for and, indeed, it is often found, thus explaining the presence of the symptom. But in other cases there is no glycosuria, nor other change in the urine, nor any cutaneous lesions which explain the pruritus. Then it has been considered as a purely nervous symptom. *But I suspect that in every case of generalized pruritus a basis of endogenous intoxication may exist, more or less masked, principally diabetic.* Hence we should not content ourselves with a mere analysis of the urine without testing by other means the possibility that the case is one of that "prediabetic" state (glycemia, alimentary glycosuria) which I have described¹² and various contemporary writers have accepted. Lately I proved this hypothesis in a few cases of which the following are examples.

CASE 46.—J. L. P. Man of forty-nine years. Robust, always well; recently grown fat and presents some changes in character (irritability, periods of sadness) which he told of himself. Slight rheumatic manifestations. *He presented a generalized pruritus, almost permanent, at times intolerable. Several urinalyses established the absence of sugar.* He was subjected to various topical treatments without result. There was no cutaneous lesion. His age and the symptoms of which he complained rather than those found on examination (hypertension 20-9, the distribution of fat, etc.) made me relate his complaints to the *virile climacteric*. There were no familial or personal antecedents in favor of diabetes or any symptom other than pruritus. While there was no sugar in the urine, *yet he had hyperglycemia (0.19) and ingestion of 150 grams of glucose produced the elimination of 10 grams in the urine in the first six hours.* He was, therefore, a *latent diabetic*, hyperglycemic. An antidiabetic diet quickly relieved the pruritus.

CASE 47.—C. de V. Forty-six years old. Always well, very strong. The menopausal crisis began at the forty-fourth year with profuse hemorrhages, loss of weight at certain times, extreme emotionalism and diarrhea. At present these symptoms persist with

¹²Marañón: Op. cit., note (1), page 18. See also the chapter *Metabolic Symptoms* in the present book.

the exception of the hemorrhages which have stopped. They are replaced by scanty and intermittent periods, appearing every two or three months. Suddenly she presented *an intense generalized pruritus* which no local or general treatment relieved. *She had no sugar but a very diabetic inheritance* (mother and aunt diabetic) and a mild hyperglycemia (0.179, fasting). This, then, was another case of *latent diabetes*. She responded well to anti-diabetic diet. In the following years she had several attacks of pruritus which always yielded to a diet free of carbohydrates.

Thus, at least in a certain number of cases, undoubtedly the *generalized pruritus of the menopause* may correspond to *prediabetic states*. These have not yet reached the stage of *spontaneous glycosuria*, but there is a *hyperglycemia* sufficient for the *impregnation of the tissues*, in collaboration with the *irritability of the nervous system*, and this causes the pruritus.

Vulvar Pruritus. Kaurosis Vulvae

Localized pruritus is apt to be chiefly vulval. It is often due to the same causes as the generalized diabetes or the prediabetic states. Again, it depends on *eczematous lesions or other dermatoses* of the genital region. *Kaurosis vulvae* and atrophic states of the external genitals coincide in some cases with an intense vulvar pruritus. According to Schickele,¹³ this occurs frequently after castration. Therefore, we may be certain that it is *a change directly dependent on ovarian insufficiency*. This is confirmed by the wonderful success which he had in one of his cases through ovarian therapy. His patient was a multipara in whom both ovaries had been removed in her twenty-fourth year. Twelve years later an intense pruritus with vulval kaurosis appeared together with an atrophy of the external genital region so intense that it was impossible to introduce the little finger into the vagina. At the end of a year of opotherapeutic treatment these symptoms had entirely disappeared and the genital region was completely normal. Block and Llewellyn¹⁴ have reported new cases of vulval pruritus cured through lutein therapy.

¹³Schickele: Op. cit., note (14), page 19.

¹⁴Block and Llewellyn: Organotherapy in Gynecology, Am. Jour. Obst. (N. Y.), 1917, p. 357. See also Chapter xxii—*Cutaneous Symptoms*.

Sensorial Disturbances

Some manifestations on the part of the *sense organs* may be presented in the critical age, such as *disturbances of taste and smell* (Schickele) *visual disturbances* and particularly various *ear noises*. All these disturbances may be purely functional, due to the climacteric crisis. But it should not be forgotten that there often appear in this age, local lesions, such as otosclerosis or cataract, which may give rise to these manifestations.¹⁵

[That sensorial disturbances are frequent during the climacteric years there can be no doubt but how much improvement in such conditions follows the general and opotherapeutic management of the case is uncertain. In my experience local lesions are very frequently found in these patients by the specialist to whom they are referred. This is particularly apt to be the case with respect to the nasal passages and the ear.—C. C.]

Dizziness. Its Various Forms in the Critical Age

Dizziness is another of the nervous symptoms of which climacteric women complain. It assumes the form of *passing* or *true rotary dizziness*, sometimes mild, again so intense that the woman must seek support but almost never falls to the ground. The dizziness may occur alone or be *accompanied by various sensations*, such as buzzing in the ears, palpitation, sensation of heat, sensation of anguish, sweating, and even nausea and vomiting. Rather frequently it coincides with the heat flushes or the palpitations studied in the previous chapter. I have seen two or three cases in which the symptomatology began and disappeared with menstrual cessation, and exactly reproduced that of *Meniere's vertigo*.

Sometimes the dizziness appears from time to time, either spontaneously or provoked by sudden movements, emotions, impaired digestion or other causes. Again, there is a state of permanent insecurity of equilibrium, with various psychic and nervous sensations, which correspond to what Tilt¹⁶ described as climacteric *pseudonarcotism*.

The *pathogenesis* of this phenomenon is probably multiple. In the first place vasomotor irritability and hypertension have an in-

¹⁵See Chapter xxiii, on *Ocular and Auditory Symptoms*.

¹⁶Tilt: Op. cit., note (10), page 102.

fluence upon it. In general those cases in which it is most intense are those with greater hypertension. The irritability of the nervous system may also have an influence and finally, as occasional causes, the digestive troubles proper to the climacteric. The fact is that in the greater proportion of cases these dizzy spells are transitory, disappearing with the attenuation of the menopausal symptomatology. Should early vascular lesions exist, the attacks of dizziness are prolonged and follow the course of that in arteriosclerosis.

Insomnia. Its Pathogenesis

Finally, let me mention *insomnia*. Very frequently women in the sexual decline sleep rather more poorly than before. According to my experience, this is almost constant, although in the greater number of cases the phenomenon is not sufficiently distressing for the patients to complain of it spontaneously. One must inquire specifically about it. But sometimes the insomnia becomes truly pertinacious, being accompanied by all the nervous and psychic symptomatology of this complaint.

Apart from the cases in which insomnia can be related to the frequent psychic disturbances of the critical age, there is another group *in the pathogenesis of which the hyperthyroid factor enters*—at least in my judgment. I have striven to indicate the importance of this factor in the menopause. My experience is that insomnia is one of the usual symptoms of hyperthyroidism. Some neurologists, like Lafora,¹⁷ believe that many cases of insomnia considered as “essential” appear in persons who when carefully examined, present various hyperthyroid symptoms. These patients when treated with antithyroid remedies are relieved of their sleeplessness which is resistant to the usual sedative drugs. In cases of climacteric insomnia I have been able to prove, I repeat, this point of view to be correct and the result of such treatment practical.

Somnolence

With less frequency women in the menopausal period *present a tendency to somnolence*, and sometimes in the postmenopausal

¹⁷Lafora: Oral communication, 1917.

period. Even taking into account that in certain cases the somnolence may be an indication of thyroid insufficiency, Marchiafava,¹⁸ Leopold-Levi,¹⁹ or hypophyseal, Cushing,²⁰ or may be due to nervous disturbances of which I have spoken, such as hysteria, the physician should look at once for the possible existence of attenuated forms of uremia, so frequent in this age.

¹⁸Marchiafava: L'iperipnia nell'ipotiroidismo. Policlinico. Soc. prec., 1911, fasc. 8.

¹⁹Leopold-Levi. Endocrinolepsias. Soc. Méd. des Hôpit. de Paris. 1913.

²⁰Cushing and Goetsch: Hibernation and pituitary body. Journ. of Experi. Med. xxii, 1915.

CHAPTER XIV

PSYCHIC SYMPTOMS. (A) GENERAL CONSIDERATIONS ON THE INFLUENCE OF SEX IN PSYCHIC LIFE

Sex Characteristics and Endocrine Glands

Without doubt we now enter the most interesting chapter of this monograph. To study the psychology of the climacteric woman is, indeed, to study the whole psychology of woman, but in the moment of its greater fullness and acuteness. The feminine organism, a little late in its development, reaches its point of maturity between the forty-fifth and fiftieth years and that part of it which serves as an organic prop to emotion, the endocrino-vegetative system, not only is mature but almost always exalted and vibrant, as we have seen in the preceding pages. When maturity is reached, life has already poured out its most important gifts—happy or sad—and the future begins to show the rays of life's sunset which is always gloomy despite a possible momentary brilliance. Then, upon this delicate and complex field suppression of the genital function occurs, an event of profound consequence. In general, man and especially woman, drags through life the chains of sex. On one side, as we have seen, sex acts in an effective and direct way upon the whole of his being. And on the other side, man himself has woven about sex a fabric of myth which makes this slavery narrower and more restricted. The fact is that throughout the whole of each human life we can easily see the traces of sex energy, not only in those activities which appear linked directly with it, but also in others—as those dependent on the physiologic life—which have no apparent relation to sex.¹ It is clear that of all sexual moments it

¹Some writers (See Valle: *Op. cit.*, note (37), page 138) oppose to this point of view the examples of the saints, philosophers and naturalists, whose sexual life has been developed in absolute chastity, such as St. Thomas, Newton and others. But it is clear that this "chastity" is referable only to the performance of the sexual act, and not to the existence of libido, which persists, doubtless, more or less dominantly, in every organism endowed with genital glands. The sublimely noble sexual sentiment is evident, for example, in the work and acts of many saints of irreproachable chastity. As for Newton, his case appears to be that of a hypopituitary condition, and his great mathematical talent fits in very well with this concept.

is the one of its extinction that leaves the deepest trace upon the nervous system which has been thus prepared.

In the first edition of this book, at this point I devoted several pages to vindicating my position as to the importance which a genital event, the climacteric, exercises upon the psychic life. In the four years which have passed since then, much progress has been made in the study of sex, in its endocrine aspect, hence all the reasons I then gave are now unnecessary. Now we know that by means of castration or ovarian and testicular grafts² we can lessen, almost erase, the sexual characters of a male or female, reducing them to the *eunuchoid* state. We can change their sex to that of the opposite one—*feminizing* a male, *masculinizing* a female. We may even hermaphroditize either one—that is, make characters of both sexes appear at the same time. And these changes, dependent on the internal genital secretion, are not limited to the morphology of the genital organs alone, but include the general morphology of the animal and also its elemental psychology, such as its libido, its aggressiveness.

We have learned then: first, that all these “sexual characters” are under the direct influence of the endocrine function of the genital gland, since the influence of the nervous system, however indubitable, is governed by the endocrines. Second, that the “sexual characters,” that is the anatomic and functional conditions which distinguish the male from the female, are not limited to the genital sphere but, as was suspected, they extend far beyond even to the psychic sphere, as I said a short time ago. Hence the female is distinct from the male, not only in the different organization of the genital apparatus, but also in her general anatomy, through her humoral make-up, through her metabolic and many of her psychic elements.

²See the literature in: (a) Steinach: Op. cit., note (14), page 31.

(b) Voronoff: Op. cit., note (21) page 31, and Greffes testiculaires, Paris, 1923.

(c) Retterer et Voronoff: La glande génitale mâle et les glandes endocrines, Paris, 1921.

(d) Tiedje: Die Unterbindung am Hoden und die Pubertätsdrüsenlehre, Jena, 1921.

(e) Pezard: Op. cit., note (22), page 31, and Le conditionnement physiologique des caractères sexuels secondaires chez les oiseaux. Thèse Facul. Sciences, Paris, 1918.

(f) Geddes and Thompson: The Evolution of Sex, 1901.

(g) Havelock Ellis: Man and Woman, ed. 5, London, 1914.

(h) But I recommend, especially, as a resumé at once complete, eclectic and balanced, of this intricate question, Athias' admirable booklet: Caractères sexuels. Lisbon, 1923.

It is clear that this differentiation is more pronounced as we rise in the scale of animal species.³ In the human species it reaches its maximum distinction although here many points appear confused through complications inherent in the superior psychology of man and through the impossibility of systematically comparing the clinical facts with experimental proofs. At any rate, I shall attempt to make an outline of the human "sexual characters" which I deem indispensable for our later study. What, then, are these sexual characters which differentiate normal man and woman?

Classification of Sexual Characters

Applying to the human species all that we have learned through animal experimentation and through direct clinical experience as recognized in cases of spontaneous lesion of the genital glands and surgical castration, we may divide *sexual characters* into *somatic* and *functional*, and both into *primary* and *secondary* groups. The most important of these appear classified in the accompanying outline.⁴ I shall explain those which are most directly linked to our present study.

In the first place, it is fundamental to note that while the genital apparatus of man is fit to accomplish the primary sexual act only in a quick and fleeting way, that of woman is also fit but through a slow, passive orgasm. This latter, indeed, is completed through those organs, uterus and mammae, which are appropriate to incubation and direct extrauterine care of the offspring. A large part of masculine and feminine psychology turns, unfailingly, about this anatomic fact. For the man, procreation is an exceedingly quick act—occupying a moment of his life. For the woman it is a series of slow, complex acts,

³See a résumé of this zoologic report in Athias' book cited in note (2h), page 186.

⁴I cannot enter here into the discussions recently brought up on the nomenclature of the sexual characters. Those interested may consult, aside from the classic works, the volumes by Havelock Ellis and Athias just mentioned, Lipschutz' review, *L'action spécifique de la sécrétion interne des glandes sexuelles*, *Revue Scientifique*, Nov. 1, 1921; the volume by this same writer mentioned in note (13), page 28, etc. I believe that my classification is the most useful of all those proposed, at least from the clinical point of view. Inasmuch as I was concerned chiefly with this utility, I did not include in my outline the humoral and metabolic characters which differentiate woman from man, perhaps more profoundly than any others, but these are now rather indefinite.

	<i>Woman</i>	<i>Man</i>		
Sexual Characters	Somatic	Primary	(a) Ovaries	(a) Testicles
			(b) Tubes	(b) Vesicles
			Uterus	Spermatic cords
			Vagina	Prostate
			Vulva	Penis
			(c) Mammae well developed	(c) Mammae atrophied
	Secondary	(a) Very unstable neuroendocrinovegetative system	(a) More stable neuroendocrinovegetative system	
		(b) Lesser development of the locomotor system	(b) More energetic development of the locomotor system	
		(c) Greater development and special distribution of subcutaneous fat	(c) Adipose tissue less developed and distributed in a more typical way	
		(d) Absence of bodily hair, beard and mustache	(d) Presence of bodily hair, beard and mustache	
		(e) Typical sexual hair	(e) Typical sexual hair	
		(f) Larynx less developed	(f) Larynx more developed	
Functional	Primary	(a) Libido toward man	(a) Libido toward woman	
		(b) Slow sexual orgasm	(b) Fleeting sexual orgasm	
		(c) Conceptional power	(c) Fecundating power	
		Menstruation (ovulation)		
		Pregnancy, delivery		
		Lactation		
Secondary	(a) Lesser aptitude for active motor impulse and for passive resistance	(a) Greater aptitude for impulse and passive resistance		
	(b) Greater sensitiveness to emotional and sensitive stimuli; lesser disposition toward abstract mental and creative labor	(b) Lesser reaction to affective stimuli; greater capacity for mental and creative abstraction		
	(c) Maternal instinct and direct care of offspring	(c) Instinct for social activity (defence and dignity of the home)		
	(d) Voice of high timbre	(d) Voice of low timbre		

which occupy, save for the minute of conception, the nine months of pregnancy, the painful hours of delivery, and the months of nursing the child. The primary functional characters are, then, much more important in woman than in man.

But this difference is found to be compensated in the greater complexity which the "secondary functional characters" reach in man. He must fulfill a part of his activities in the social medium, those which are necessary to the defense, sustenance and progress of the home and of the care of the offspring when this lies outside maternal care. These are activities which in normal conditions do not correspond in any way to woman's activities, neither in point of time, or anatomic and physiologic constitution. Thus, then, the sexual character of these activities of man is indubitable. We may call them, as a whole, "social activities" and include therein all those diverse acts performed in the elementary struggle by primitive man or the present-day savage for the procuring of food and the defense of the home from other men, from wild beasts and the elements, up to the complex means of modern struggle for existence in all its financial, industrial, commercial and professional aspects. Just as sex has imposed upon woman the apparatus for incubation and nourishment, of which it has deprived man, so sex has imposed upon him the somatic characters, of nutritional type, a greater ruggedness of the skeleton and of the muscular system, of coarseness of the neuroendocrine system which make him particularly fit for those diverse forms of the struggle for existence which are equivalent to maternal activities.⁵

Social Activity and Sexual Feeling

This "pansexual" conception of the respective activities of either sex, bring within the sexual sphere the most elevated

⁵One of the interesting consequences of this point of view, which I may only indicate here, is that it permits us to get the problem of feminism into focus from the biologic angle. See my essay, *Biología y Feminismo*, Madrid, 1920. The activities of woman, like those of man have within normal physiologic limits, an impassable barrier, in the biology of each sex. It is clear that these barriers may be broken. In fact, nature has broken them many times, and an education directed to this end could violate them more or less. But nature has balanced and will continue to balance attempts to go outside these normal limits. That is to say, these attempts will be limited to exceptions, since all that is monstrous and pathologic is exceptional. The problem of feminism, fortunately, has remained of late years within its true limits, reduced to a merely legislative and social question, of which there can be only unanimous approval.

psychic functions, which, nevertheless, cannot be considered as strictly "sexual characters." The development of the cerebral functions, through the evolution of humanity has liberated the human mind, little by little, at least in a certain number of individuals, from direct dependence upon the fundamental instinct of perpetuating the species. But the roots of each sex, buried in this primitive stratum, continue sending their specific sap to that tall and leafy tree, the mind of modern man. Woman has found, especially when through social or organic reasons she has not become a mother, various noble activities, such as teaching, the care of the sick, certain industries, professions and arts which require manual dexterity and careful attention, which are free from unforeseen conflicts, and which are but modified extensions of some of her primary functions. And man, from the multiplicity of his duties and activities connected with the gaining of a daily livelihood, rises through the higher professions to the pursuit of science and the arts, and finally, to mental creation, which as the highest expression of the human spirit is, in my judgment, and under physiologic conditions, a typically masculine function.⁶ It would be most interesting to study this evolution of masculine social activity which can be only indicated here. It is unquestionable that the direct defense of the offspring and the home proper to primitive peoples, is transformed with the progress of humanity into the struggle to acquire arbitrary values, like money, with which food is bought and service is paid. Latterly two new elements have been added, which complicate the social activity of man, avarice and the thirst for glory; that is, the hunger for more money than others have, in order to dominate, or to live better, or simply for the pleasure of hoard-

⁶Therefore, the creative power is given, in typical conditions, only to the man. The sexually normal woman is, through the constitution of her organism, unfitted for creation, as she is extraordinarily fitted for copying, preserving and slowly perfecting norms already established. In this respect there is an interesting fact brought out by the unfortunate Gomez Ocaña (a) *El sexo, el hominismo y la natalidad*, Caleja, Madrid, 1926—This is that in the Art museums, statistics show a great majority of copyists belong to the feminine sex. Nietzsche said that "when a woman has scientific talent"—that is, aptitude for mental abstraction and creation—"there is something in her sexuality which is not well defined." (b) *Nachgelassene Werke*, 1881-86. The same idea thus expressed aggressively by Nietzsche has been developed by:

(c) Weininger: *Sesso e carattere*, Italian edition; Fenoglio, Milan, 1912. See also:

(d) Mœbius: *Ueber die Wirkungen der Kastration*, 1903.

(e) Metschnikoff: *Essais optimistes*, Paris, 1907, The literature on this point appears interminable.

ing it, and the desire to prevail over other men by means of a recognized superiority, physical or mental. In varying degrees and in different ways, these two, money and glory, are the impulses behind every human action, and we can easily see how they are derived directly from a sexual function. Many of today's commentators revolt against this tendency to subordinate the majority of human acts to the influence of sex. But it is not enough to protest. The contrary must be proved. For the moment this theory of pansexualism is useful to us because these objects of human activity, money and glory, are converted into magnetic poles of sexual attraction. The man knows that through triumph the field of love will be made easier and the importance of money in that field is well known. We shall see presently how it plays a rôle very close to biology in the intersexual struggle of today. It is true that another instinct, that of conservation, is the motive of another large group of human actions, including many of those which I have cited as influenced by the sexual instinct. But that does not contradict the theory which I have just sustained. The instinct of self-preservation and the sexual instinct are not opposed in their roots. Their relation is as close as that between the individual and the species. And it is difficult not to find traces of either in the acts which are directly related to each.

All human activity, from cellular up to mental endeavor, is then, influenced by sex. Nor is it surprising that psychic repercussions of sexual functions should be mentioned. The clinic confirms the diary, teaching us the exact parallelism existing in both men and women of the various physiologic and pathologic episodes and sexual activity and the psychology of each individual. The ideology and the emotional context of a man or woman are different before and after puberty. During sexual maturity they also vary in the heights and depths of intersexual commerce. They vary, too, when the normal decline of the reproductive organs, the climacteric, occurs. If these organs suffer lesions which disturb their function, or if they are extirpated by the surgeon or for other reasons as in eunuchs or present-day skoptsy, the morphologic changes which the organism experiences are closely united to certain psychic changes. And all these changes point

in the same direction. When the internal genital secretion does not act, the psychology has something of ambiguity about it, something of the hermaphrodite, like the morphology. It is by means of this secretion that sexual differentiation is effected in the sense that I explained before—that is, following the direction of masculine or feminine sexual characters.

Sex Types and Blurred Sexes. Sexual Perversion and Organic Hermaphroditism

Up to now I have referred solely, and this is important, to *sexually normal cases*. Or, speaking more accurately, to cases which are *sexually typical*, since in speaking of sex we must be very cautious in applying the adjectives “normal” and “abnormal.” *Within normality, by the side of typical cases of femininity and masculinity, there is a considerable group of cases wherein sex is not clear and which react in their own way under the stimuli playing on sexual life. And even individuals of perfect sex may appear at certain moments not only with a lessened sexuality but with a frankly heterosexual inclination.*

Formerly, everything that was heterosexual, everything in each individual which reminded one of the opposite sex, was considered as an abnormality—disease, monstrosity or vice—pathologic and wicked. Today we look at the problem in a very different way. *All modern sexual psychology should be informed on these principles: (1) The human embryo is primitively bisexual. (2) That each man or each woman possesses his respective sex, not dependent on an organic, qualitative, fundamental difference, but on simple quantitative factors; so that one sex or the other acts with greater force upon the bisexual embryo and at last prevails. (3) But we all conserve, dormant, seeds of the opposite sex, which can be reactivated in certain moments of life and leave their tardy heterosexual traces upon the already formed organism. Finally, between the perfect masculine type and the perfect feminine type, and the hermaphrodite exhibited in side-shows there is only a qualitative difference, since, as I have said, they are simply the opposite ends of a chain. Between these extends a multitude of intermediate sex types, without our having any exact means of determining where the normal leaves off and the pathologic begins.*

[Bell* calls attention to a fact not to be forgotten that "Man is dimorphic and that the prominence or otherwise of the secondary characteristics depends on the degree of masculinity or femininity present in any given individual." While the dominant characteristics usually indicate the declared sex of each and the recessive characteristics remain more or less latent, we find individuals in whom masculinity becomes evident in the female and femininity in the male.—C. C.]

It is curious to note that these transcendental conclusions have been reached by two distinct and independent routes, the psychologists (particularly the Freudian school) on the one side, and the physiologists and endocrinologists on the other. One of the most important conclusions, in my judgment, reached by the psychoanalytic theory is that⁷ of considering as normal in almost all individuals a certain degree of psychic bisexuality or sexual perversion, that is, of the instinct for attracting the same sex. I believe it is an obvious exaggeration to say, as Freud does, with little delicacy, "that it may be stated that the erotic feelings directed towards persons of the same sex, in the psychic life play as important a rôle as those directed toward the opposite sex." This is not so. There is in each man and in each woman, a germ, hidden and sleeping, of homosexuality, which, in normal circumstances, is inclined toward the same sex, and which, on exceptional occasions, may be revived. This should not be overlooked in the present state of science. And it would be better if each would meditate seriously and without prejudice upon the problem, instead of avoiding it with consternation or questionable witticism.

In short, this germ of bisexuality (I do not speak here of perversion) is the psychic equivalent of the organic bisexuality to which I referred before, and no one should now be in the least doubt about it. Freud's error is precisely this one of not wishing to relate his "original psychic homosexuality" with the "original organic homosexuality," thrown into relief by the endo-

⁷I have referred several times to Freud's ideas. Those who wish to amplify their knowledge upon this material may consult the recent translations (*Trois essais sur la théorie de la sexualité*, Paris, 1924) and (*Obras completas del Profesor Freud*, translated by Lopez Ballesteros, on the press.) Also the various critical contributions on the subject by the majority of our neurologists. (Fernández Sanz, Lafora, Valle Aldabalde, Sacristán, Villaverde, Sanchis Banus, etc.)

*Bell: Op. cit., note (30), page 21.

crinologists. In the fourth edition of his *Drei Abhandlungen zur Sexualtheorie* (Wien, 1920) he states that "there are those who say that somatic hermaphroditism and psychic inversion are two independent things," notwithstanding the studies of Lipschutz and other physiologists on the internal genital secretion which he cites, for the first time, in his final notes. Freud's argument is that "often" psychic homosexuality is not accompanied by manifestations of organic homosexuality. But this statement is open to discussion and cannot be made without documentary proof. *Perhaps inconstantly and even rarely does sexual perversion coincide with the large salient and showy manifestations of organic hermaphroditism, those which can be seen at a glance without the necessity of a medical examination of the individual. But a long and attentive study of the cases of homosexual perversion which have received medical observation brings out the existence of minor hermaphroditic signs.* These are, in men, smallness of the external genital organs, as stressed by Havelock Ellis,⁸ sexual hair of feminine type, unmasculine bony and muscular morphology, scantiness of the beard and mustache, feminine distribution of fat, higher timbre of voice and so on. In women the contrary signs appear, such as overdeveloped clitoris, masculine sexual hair, tendency to hair upon the body and face, and very energetic locomotor system.

Moreover, I have been able to prove, in some cases, that these somatic manifestations of hermaphroditism are appreciable as such only in prepubertal years, later being extinguished wholly, or almost wholly, but the homosexual tendency of the instincts is conserved, or at least leaves the individual predisposed to its revivification. I recently published a study of some such cases, which are much more frequent than believed, under the name of *prepubertal pseudohermaphroditism*.⁹ In these, the "secondary sexualism"—femininism in men, masculinism in women—did not make its appearance somatically but only in times of crisis in the organism, particularly in the prepubertal period. The "primary sexualism" was later asserted especially if helped by

⁸Havelock Ellis: Op. cit., note (2g), page 186.

⁹Marañón: Pseudohermafroditism prepubertal, Conferencia en el Colegio de Médicos de Santander, December, 1923.

proper treatment. There will always be, in the course of life, cases due to errors of instinct, particularly if compelling circumstances arise. Therefore, let us repeat, the various cases of homosexuality studied and which were more or less manifested, did not have, indeed, physical signs of hermaphroditism but there had been this prepubertal transitory phase of it.

Likewise the other case exists—that is, of individuals with the anatomic features of hermaphroditism, more or less complete, more or less marked, with a clearly normal heterosexual instinct. And finally there are cases *wherein the inversion appears in only one of the sexual characteristics*, either somatic or functional. For example, there are women with a marked development of masculine hair and yet are otherwise very womanly in their anatomy and in their psychology. Or there are men, very masculine as a whole, with the exception of a morphologic detail, such as feminine distribution of hair, or a psychologic trait which is not very masculine; for example, inability to take part in social activity and an excessive amatory predilection as occurs in those of the Don Juan type. *This does not mean that all the sexual characters are reversed, but that inversion may be confined to a single group of them, or to one character alone, the rest remaining true to type. This is partial inversion.* Later I shall attempt a classification of sexual inversions based upon this point of view. All these concepts, upon which I may have enlarged at too great length, must be kept in mind in order to understand some of the psychic changes as well as the somatic which appear in the critical age and following surgical castration. Especially is this true in the former, since in the revivification of the latent germs of the opposite sex, not only the suppression of the genital function seems to intervene, as I said in Chapter IV, but also a collaboration of other glandular disturbances, hypertrophy of the supra-renal cortex perhaps, which occurs in the physiologic climacteric and not in surgical or in early castrations.

Finally, it should not be forgotten that *in man, especially at maturity, all the psychic changes of genital origin are influenced by the nervous system which can modify up to unbelievable limits the pure consequences of a certain genital lesion.*

Psychic Disturbances and Other Internal Secretions

Besides the internal sexual secretions, in this complete sense, the internal secretions of the thyroid, the hypophysis and perhaps as well as the suprarenal, thymus and parathyroid all act upon the psychologic sphere. A great number of recent works establish this relation between psychopathic states and endocrine disturbances with great precision, particularly, Parhon,¹⁰ Borchardt,¹¹ Bauer,¹² Marburg,¹³ Rodriguez Laflora,¹⁴ Cushing,¹⁵ Dumas,¹⁶ Fernandez Sanz,^{17, 18} and Sanchis Banus.¹⁹

Finally, it is understood that the endocrine crisis of the menopause, wherein not only the genital glands are profoundly altered but also, nearly always, the thyroid and the suprarenals, gives rise to frequent psychic disturbances. We shall now examine these from this pathogenic point of view.

¹⁰Parhon: Cercetari asupra glandelor ou secretione interna in reportal lor ou patologia mentala, Bucaresti, 1910.

¹¹Borchardt: Die Bedeutung der Hormone für die innere Medizin, Beiheft. für Med. Klinik, 5, 1911.

¹²Bauer: Neue Untersuchungen über die Beziehungen einiger Blutdrüsen zu Erkrankungen des Nervensystem. Zeitsch. für die gesammte Neurologie und Psychiatrie, 1911, iii.

¹³Marburg: Jahreskurse für aerztliche Fortbildung, 1912.

¹⁴Rodriguez Laflora: Locura maniaco-depresiva e hipertiroidismo Rev. Clin. de Madrid, 1913-14.

¹⁵Cushing: Psychic disturbances associated with disorders of the ductless glands. Am. Jour. Insanity, 1913, lxix.

¹⁶Dumas, G: Curso de psiquiatria. Junta de Ampliación de Estudios, Madrid, April, 1924.

¹⁷Fernández Sanz: Las secreciones internas en su relación con la patologia mental. Progresos de la Clínica, 1914.

¹⁸Fernández Sanz: Las secreciones internas en su relamiento y la patogenia de las psiconeurosis. Inaugural address: Academia Médico-Quirurgica, 1917-18.

¹⁹Sanchis Banus: El estado mental de los eunucoides. Archivos de Med., Cirugia y Especialidades (Madrid) Nov. 10, 1923. In this article there will be found a resumé of the present state of the question with comment on hypogenital mentality and its social value.

CHAPTER XV

PSYCHIC SYMPTOMS. (B) USUAL CHANGES IN CLIMACTERIC PSYCHOLOGY

Psychic Symptoms and Psychic Complications of the Climacteric

First of all, let us divide this psychic symptomatology of the climacteric into two groups. These are, indeed, difficult to delimit, let me say at once, in order to forestall certain criticism.

In the first group we shall include some psychic changes which may be considered as directly dependent on the endocrine crisis. These are, therefore, *psychic symptoms* which are transitory like the crisis itself. They do not have the definite clinical structure of the psychopathies properly speaking, but they have the vagueness of mental and marked emotional states which bring the normal psychology of the individual into this ambiguous zone wherein the human spirit is frequently agitated—where the normal and the pathologic have only circumstantial value. In the second group I include the definite *psychopathies and neuroses* which may occasionally appear in the menopausal field as *complications* of it. We may compare the psychic situation of the first group, which Regis¹ called *elementary psychic disturbances*, to the vasomotor upsets, to the suffocations within the characteristic circulatory symptomatology. That is to say, these disturbances, in a restricted pathologic sense, may be considered practically as normal symptoms of the menopause. On the other hand the states of the second group, as I have said, are *true complications* of the climacteric, comparable therefore, without leaving the example of circulatory pathology, to the arteriosclerosis or the hyposystoles which are sometimes observed in women in this age. And just as these circulatory complications presuppose the antecedent existence of a cardiac or vascular lesion so, too, climacteric psychopathies only appear, according to all probability, in women whose nervous systems have a frankly pathologic predisposition, as we shall see presently.

¹Regis: Précis de Psychiatrie, Paris, 1909.

The changes in the first group are those which will interest us especially. The most frequent are those directly related to the organic disturbance of the menopause and, therefore, especially characterizing the climacteric psychology. Among them we shall study, on the one hand, *emotional instability*, and on the other, the *modifications of sexual feeling* produced by the subsidence of sexual life. As complications we shall concern ourselves with *psychopathies and neuroses*. I explain this division schematically in the accompanying outline.

Psychic symptoms	{	Emotional instability	{	Exaggerated diminution of sexual feeling
		Changes in sexual feeling		Sexual sadness
				Increase of sexual feeling
				Inversive tendency
Psychic complications	{	Psychopathies properly speaking	{	Mania
				Melancholia
				Manic-depressive states
		Neuroses	{	Neurasthenia
				Hysteria
				Epilepsy

Emotional Instability of the Critical Age

Emotional instability is an element common to almost all menopausal women, and therefore, the most characteristic. *Often it is the only psychic phenomenon of the menopause.* Again, it coincides with, and serves as a foundation for, the other disturbances to be mentioned later. In Chapter IX we saw that the endocrine change of the climacteric causes a state of acute and exquisite sensibility of the woman to emotional stimuli. Perhaps the first early manifestation of the menopausal change is this emotional irritability in the woman, which is perceived at once by persons about her and then by the patient herself.

At times, the coincidence of the emotional state with the menstrual disturbance is so noticeable that the pathogenic relation of the two phenomena cannot be doubted, as in the following example:

CASE 48.—M. F., forty-nine years old, unmarried. Of normal character, always very calm. Without previous illness. The menses, normal until then, suddenly stopped two months prior. From then on she perceived, along with a "sensation of congestion," suffocation and other clearly climacteric symptoms, an *extreme and causeless emotionalism*. On coming to my office she burst into tears without knowing why. Arterial tension at this time, 19-10. A moment later she was calm and the tension had fallen to 17-9. Examination and analysis negative.

This emotional instability is manifested in varying intensity in different cases, from simple changes of character which are scarcely perceptible up to permanent and intense emotional states. All the emotional stimuli—sadness, joy, fear, impatience—put the organism of the climacteric woman into vibration which may be violent. Bad news affects her profoundly, even when it does not directly concern her. A sad tale, which others hear with indifference, makes her weep. This increase of emotionalism can often be clearly seen in the theater, where the dramatic moments to which she was formerly indifferent now fill her eyes with tears. The same is true of joyful emotions, although, in this age, these are less frequent and the soul is less favorably disposed toward them. The emotion of fear is also exaggerated and we often see women, who were formerly serene, become apprehensive and cry out at some unexpected noise or at any other small cause.

Better than any description the following paragraphs give an idea of this peculiar psychic state. These are copied from a letter written by a very brilliant and observant woman who had always been well balanced. Now she had been seized by disturbances attributable to an early climacteric.

"Why has my character changed so much? Formerly I was very calm and now a vexation or an injustice produces in me such discomposure—so strong an emotion dominates me that others can tell it by the tremor in my voice. And I especially notice what seems to be a feeling of horrible anguish—a sensation like oppression—as if my heart (to speak unscientifically) threatened to leap from its place. What worries me most is that this excess of emotionalism is not related to causes, since if

I hear something sad—no matter how sad it may be—my usual calmness is not altered in the least. Why am I fearful, if nothing threatens? My greatest diversion used to be to walk alone to my house in the country and to be left there alone in peace. Now, I go as before. But when I find myself alone there I am afraid and not of anything, but rather of myself.”

But this disposition of the climacteric spirit is particularly manifested by *impatience over trifles*, upon which I shall comment briefly.

Climacteric Impatience. Examples.

Impatience is, indeed, of all the signs dependent upon emotional irritability, the one which most often characterizes climacteric psychology. In many cases this irritability precedes all other menopausal symptomatology by many years. At times it arises from the slightest causes in everyday life which succeed in making life very hard for her associates, chiefly the most intimate ones, husband, children, and servants. I prefer to copy some examples here from literature, which are as exact and less distressing than the countless ones of real life. In Feuillet's comedy *La Crise*,² which, aside from its disputed literary merit, contains many observations based on an excellent knowledge of feminine psychology, as Prevost³ says. Julia, the heroine, is a woman who has been well-balanced. She is now in the fullness of her sexual life and therefore within the shadow of its close. She makes these characteristic reflections.

“What name can be given to this moral affliction, to this discontent with myself and with those about me which I have felt for some months. My husband is, doubtless, the best of men. But nothing that he says or does pleases me. His watch charms irritate me above everything else. Yet these charms and I have lived together in peace for ten years. Then suddenly, one fine day, we hate each other. My husband has the insufferable habit of jingling them while he is talking—making an unbearable clinking. At the very instant that I write these lines he is in his room, winding his watch and making a noise with those charms.”

²Feuillet: *La Crise*, comedy in four parts, Paris, 1882.

³Prevost: Introduction to the French translation of *L'Age Dangereux* by Michaelis, Paris, 1911.

As clever and picturesque as these words, are those in which Julia's husband, M. De Marsan, a dignified magistrate now thoroughly alarmed, reports to the physician the change which he observes in his wife. These words give to the very life so actual an experience that, without questioning him and without knowing the intimate life of the author we are inclined to pity him.

"It is not," he says, "a question of extravagant symptoms which would attract the attention of outsiders, but of shades, each day more marked, which do not escape an intimate like myself. For ten years I have said I possessed a treasure in my wife. Then suddenly this sweet Julia takes on the air of a martyr—obedient, but irritated. This woman of the world, this refined woman now speaks a language full of sharp, bitter words, harsh and peevish maxims. I find in her conversation—previously so mild—a banal melancholy, a sharp poetic flavor, with a socialistic tendency which fills me with uneasiness."

The physician then interrupts.

"The wife of a magistrate! Horrors!"

M. De Marsan continues his remarks and ends thus:

"At the same time that the woman changed, the mother changed too. Her husband is now a tyrant, the children a heavy burden. She scarcely speaks to them. They are left to themselves. Here, then, doctor, is what has happened to me. Here is the crown of thorns which Julia has put upon my innocent head, without the least provocation on my part. What is the explanation?"

And the wise doctor comes to the point:

"Perhaps I have it—your wife's age."

In Michaelis' admirable novel, *L'Age Dangereux*, which I shall quote, numerous observations are found, doubtless personal, expressing this same characteristic state of irritability in menopausal women. This particular woman whom I shall mention several times runs away from her home on reaching the "dangerous age," driven by a state of mind which she describes in her diary. Her remarks are deeply touching. Once, in speaking of her husband, she says :

"The sight of Riccardo slowly became a torture to me. With

what absolute perfection he managed his knife and fork! I could have stood it if he would ever—if only once—put his elbows on the table, or bite into an apple before peeling it, or make a noise when drinking! But no: his correctness was infallible and unchangeable!”

And farther on:

“His mania for correctness drove me to committing every possible solicism, just to annoy him. Sometimes I purposely disarranged the books in his library. And then in five minutes I would put everything back in its place.”

Very often, as I have said, this state of irritability centers on the husband, or the lover, doubtless because he is the nearest one in the sexual orbit. But it may also be directed against outsiders, as the servants. This frequently happens in Spain, no doubt because of the indolence of the domestic servants of the middle class.

Endocrine Pathogenesis of Emotional Instability

The close relation between this emotional state and the endocrino-vegetative instability in the early stages of the climacteric cannot be doubted. In a recent paper on *Age and Emotion*,⁴ I wrote at length on this point. Hence I refer the reader to that article and to Chapter IX of this volume. Let us also remember that an increase of emotional attacks appears in this age, in the majority of cases linked to this increased predisposition. Far from dulling the emotional aptitude as is commonly believed, this age renders it more acute and sensitive. “The heart,” we say metaphorically, “like fruit, ripens under blows.”

I have said “the early stages” since this emotional predisposition usually lasts but a short time and may soon be replaced by a normal emotionalism and then a state of blunted emotion follows.

Psychic Serenity in the Menopause

As already noted, in a great number of women mental disturbance in the climacteric is limited to this emotional instability.

⁴Marañón: Op. cit., note (1c), page 87.

When the neuroendocrine crisis does not exceed certain limits of abnormality, when the woman's nervous system has no marked psychopathic predisposition which carries her away under unusual stimuli, when her sexual life has unfolded without clashes between instinct and environment, fortunately the case with the majority of women, then these emotional upsets disappear and the spirit enters upon an era of peace which is only disturbed by purely intellectual reminders of the past. This state of autumnal peace may be wholly harmonious and happy in many women and men, who perhaps until then never acquired organic, and therefore psychic, equilibrium. In my essay I made mention of various opinions concerning this conclusion. Let me recall here, since it corresponds to one of my observations, that of Madame de Hauville⁵ which may be perhaps too enthusiastic to be entirely sincere:

"Do not remind me of my youth. I believe that maturity and old age which it initiates is the perfect moment in which one hoards and remembers. Then all the splendors of the world appear finer. The close of life is undoubtedly more beautiful than its dawn."

Let us also note Michelet's⁶ well-known lines on *the rejuvenation of love* in contrast to Nietzsche's⁷ lines which are so far from the orderly and somewhat over-sweet optimism of the French writer.

"The autumn of life is an epoch full of the mystery of all that is unperturbed. It is similar to a wide plateau on a mountain-top, swept by a fresh breeze, beneath a fair and cloudless sky, whence the earth is contemplated with equal serenity by night and by day. It is the stage of recollection and most sincere happiness."

Disturbances of Sexual Feeling

But just as, in a great many cases, the genital phenomenon, menstruation, disappears with fluctuations and changes and not through an insensible graduation, so sexual feeling is also quenched abnormally in some women. *Sometimes this abnor-*

⁵Cited by Esteve: *L'hérédité romantique*, Paris, 1919.

⁶Michelet, *L'amour*, Paris.

⁷Nietzsche: *Le voyageur et son ombre*. H. Albert's French edition, Paris, 1915.

mality is due to irregularities in the endocrine reactions which serve to excite it, sometimes because of the exaggerated way the nervous system reacts. These give rise to different complex disturbances of sexual psychology, truly characteristic states, without becoming real psychopathies properly speaking. These states, as I have said, constitute with emotional instability, the foundation of climacteric psychology. They may be classified into four basic groups: (a) *exaggerated diminution of sexual feeling*, (b) *sexual melancholy*, (c) *increase of sexual feeling*, and (d) *tendency to sexual inversion*.

(a) **Exaggeration, Diminution of Sexual Feeling. Aversion for Men.**—Gradual lessening of the sexual impulse is normal in the menopause. It is a simple example of the physiologic phenomenon whereby the disappearance of the organ is always followed by the loss of its function. The examples which Schickele⁸ recalls, of male animals after castration not seeking the female, show this. The periodic sexual impulse may be made to reappear by ingrafting testicles. Pezard⁹ has demonstrated this in chickens, Steinach¹⁰ and others in the guinea pig. Castrated females have been observed to resist the male vigorously. The phenomenon is clearly seen among animals where there is only the instinct of sexual attraction.

But in man sexual emotion is much more complex since upon libido itself is imposed all the psychic element of love, the reactions of which are very complicated. Yet in many cases of this aggressive reaction to libido, the most simple of all, the spiritual complexity of the phenomenon is brought to view. Sometimes, indeed, *the suddenness and the intensity of the quenching of sexual attraction which may be converted into sudden and profound aversion for the opposite sex* indicates, as Walthard suggests,¹¹ the intervention of a psychic element in the symptomatology.

I have seen this type of psychic reaction, especially in women who have had many children, and an existence wholly devoted

⁸Schickle: Op. cit., note (14), page 19.

⁹Pezard: Op. cit., note (22), page 31.

¹⁰Steinach: Op. cit., note (20), page 31.

¹¹Walthard: Der Einfluss des Nervensystems auf die Funktionen der weiblichen Genitalien. Praktische Ergebn. der Geburt. u. Gynäk., 1910, ii.

to the home, deprived of the sexual suggestions of so-called "society life." In these women, especially when they have very exaggerated religious ideas as is frequent in the Spanish middle class, the absence of menstruation brings the feeling that her sexual life has ended. So violent is this idea that it brings actual repulsion, sometimes instinctive, through conscientious scruples. This sudden change in the woman may be the cause of serious domestic conflicts when it surprises the man in full amorous activity, as it frequently does. Metchnikoff¹² in studying the *disharmonies of human nature*, forgot this frequent and interesting aspect of sexual disharmony which the menopause is apt to bring. It may happen, too, that this aversion reaches not alone to the nearest man, the husband, but to all the opposite sex. I know of one woman who feels a veritable aversion for men in general while retaining, on the contrary, an affection for her husband. Michaelis describes the same thing in his novel. The mere presence of the gardener, the only man she allowed to enter her retreat, produced physical distress in the heroine, while the passion her lover inspired was heightened.

This loss of libido may *even render the sexual relation intolerable to the woman*, producing those true nervous disturbances which cause the woman to seek medical aid. I have seen three such cases wherein the women conquered their aversion, either through a sense of conjugal duty or for professional motives.

(b) **Sexual Melancholy.**—*Sexual depression*, the second of the abnormal psychic elements in the critical age, is *a state of psychic depression originated by the loss of sexual function*, independently of the loss of libido and with which it should not be confused. The latter is concerned with a phenomenon which is principally instinctive, the former with a phenomenon chiefly psychic although it is clear there is no radical division since obviously they are very close together. *It is thought that the lack of the ovarian hormones, through a merely humoral mechanism, may cause an impoverished psychic effect in women whose ovaries have functioned actively until this time which is comparable to that of the sudden deprivation of a chemical substance to which the organism has been accustomed.* In women who have been castrated

¹²Metschnikoff: *Etudes sur la nature humaine*, Paris, 1905.

in full youth this is observed with greater clarity. But at any rate the change which we are studying *depends essentially upon psychic factors*, which are worthy of comment.

The *sensation of realizing that one is ageing*, of losing the ability to attract the opposite sex which the woman associates with the phenomenon of menstrual cessation partly because of its biologic significance and partly because it sometimes coincides with irrefutable evidences of advancing years—gray hair and wrinkles—produces in some women an interesting order of psychic phenomenon of depressive type. This I call “sexual melancholy.” These disturbances are especially observed in those numerous women who live an intense life, society women and prostitutes of all kinds to whom sexual success is either an explicit or a subconscious means (an honest exhibition of her beauty, her elegance, her handsome clothes) and the principal end of her existence. The woman who reaches the menopause surrounded by her children and who has the care of her home, may consider the object of her life accomplished and accept the loss of her reproductive power in an attitude which I have called “psychic serenity.” For this reason, the menopause is apt to be less turbulent from this psychic point of view in women of the poorer classes. In the upper classes sexual suggestion is much more acute and frequent. Icard¹³ and other writers have made a sentimental parallel between these two classes of women which I do not care to repeat. Whatever her station, this calm at the close of sexual instinct is favored by the exercise of the woman’s intelligence, artistic abilities or simply by active labor in the professions or any duties which completely absorb her interest or divide it with household cares. Finally, this calm is common among those women who, restrained by religious ideals, have succeeded in relegating to second place the fluctuations of their organic functions. I have repeatedly verified the enviable spiritual peace with which nuns pass through the climacteric crisis despite intense suffering through such bodily distress as suffocation and palpitation. For the same reasons, this class of psychic disorders is less frequent and less marked in man. In him, when his sexual organism is

¹³Icard: Op. cit., note (18a), page 108.

perfected, primitive sexual success is always secondary, and the roads leading to other forms of social satisfaction, which we considered as of secondary sexual nature, remain open and even widen in this age wherein man frequently reaches the maximum point of his activities.

For the woman who has only sought and only satisfied herself through sexual means of whatever sort, the coming of old age brings an abrupt transition from happiness to misfortune which fills her with veritable grief. "Old age" and "growing old" constitute an obsessional preoccupation in these women. This may give rise to true psychopathic states, such as *mysticism* and *isolation*. In Spain *exaltation of religious ideals is especially frequent*, either in the form of *pure mysticism* or that of *religious organizations or pharasaic charity*. This spiritual exaltation of women, on the other hand, occurs much less frequently in other countries. There the spiritual exaltation which is of a compensatory character takes other routes, which are little in harmony with the mentality and education of Spanish women, such as various *philanthropic activities, ethics, or politics*. Let us recall the "socialistic tendency" which so alarmed the husband in *La Crise* in the scene given above. From the time of Feuillet down to our own, this phenomenon has been very marked and it has been alluded to repeatedly, although never scientifically, in connection with the exalted actions of the English suffragists as due to the influence of a sexual disturbance of a hypogenital type.

Isolation, self-seclusion, on the woman's part, through the melancholy realization of growing old, is apt to be more marked in the psychopathic states which we shall study next. This prototype is found in *L'Age Dangereux*, so often mentioned.

(c) **Increase of Sexual Feeling.**—Very suggestive is the study of the third of the states which we are discussing, that is, the *increase of libido and of sexual feeling in the climacteric*. It is a matter of common observation that at this age women's sexual emotions frequently revive and they launch out into love adventures, perhaps for the first time in their lives. This fact has been much exploited in literature. Organic and psychic factors explain this change, as they explain the others we have studied.

(d) **Hyperoöphorism and Ovarian Instability.**—Let us recall

the theory, held by Pende¹⁴ and others, that before the extinction of the ovarian function, there is a recrudescence, a phase of *hyperoöphorism*. This is clinically manifested by the copious menstrual periods which in many cases characterize the preclimacteric stage and to this assumed hyperoöphorism is attributed the amorous outburst. I have already refuted this hypothesis which no other indication authorizes us to accept. The theory is incompatible with the fact that the increase in passion does not always coincide with the early stages of the menopause. The increase in passion sometimes does not appear until the menopause is far advanced, and it lasts for a long time after the activity of the ovary has been definitely extinguished. *But although there is no clear hyperoöphorism, we can say that the internal secretion of the ovary is poured out irregularly, fragmentarily, corresponding to the state of "functional instability" which characterizes its last moments of activity.* Blair Bell¹⁵ expresses this very exactly in speaking of the "irregular emission of the ovarian stimuli in the menopause." And with this endocrine change there doubtless collaborate the other internal secretions which are altered in this age. Of these the chief is hyperthyroidism which, aside from the cases wherein it produces a predominantly asthenic symptomatology, excites all the appetites, among them the sexual. I base my theory of this organic foundation, ovarian and thyroid instability, upon the fact *that it is almost never presented in women who have been castrated in youth.* In these the internal secretion of the ovary is suddenly suppressed and the other glandular reactions are not of the same type as those which occur spontaneously in a menopause which is chronologically physiologic.¹⁶

¹⁴Pende: Op. cit., note (17), page 19.

¹⁵Blair Bell: Op. cit., note (30), page 21.

¹⁶Nevertheless cases are cited (Glaevecke: Körperliche und geistige Veränderungen im weiblichen Körper nach künstlichem Verluste der Ovarien. Arch. f. Gynäk., 1889, xxxv.) of persistence of sexual desire in women after castration, similar to that observed in some eunuchs castrated after puberty. Lately several writers have dwelt on this phenomenon evaluating what is endocrine and what is nervous in libido and its realization. In my judgment the explanation depends on three factors. (a) In the first place it depends on a fact which writers have not stressed, and which I believe is vital, to wit:—that accessory genital tissue escapes extirpation. This continues supplying the internal genital secretion. (b) Moreover it is possible that the action of the internal genital secretion *impregnates* (eroticizes, Steinach says. Op. cit., note (20), page 31, the nervous system and this impregnation lasts for some time after castration. (c) Finally, there are those who admit, for a group of cases, that the sexual desire is purely mental elaborated by the memory

Pruritus and Local Lesions as the Cause of Sexual Disturbances

Other agents still more organic and causing this sort of climacteric disturbance are *vulval or vaginal lesions and irritative conditions or eczemas, producing a local hyperesthesia*. Such states may lead to impulsive search for sedation through any means whatsoever. Boerner cites uterine lesions, fibromas or hypertrophies, as another cause of sexual excitation. There are many such examples in the literature on the menopause and I could give several myself. *Even without any lesion there can be an extraordinary hyperexcitability of the delicate and numerous nerves in the external genitals which receive the voluptuous impression of contact perhaps through circulatory states, as local plethoras*. Numerous cases have been reported of women who throughout their sexual lives have always been indifferent to the physical pleasures of love, a very frequent occurrence as is well known, and who, on reaching the period of sexual subsidence, experience it in all its intensity, sometimes morbidly so.

I have frequently observed that this sexual hypersensibility is *localized in the nipples*, as I indicated in Chapter XI. The mammary region is often the seat of erotic reflexes among women whose primary genital apparatus lacks sensibility.¹⁷

Psychic Causes of Hypersexualism. The Desire to Experience Sensations Which Are About to End

Besides these *organic reasons* for hypersexual disturbances, there are the *psychic* which are also related to the organic period of the crisis although not directly dependent on it. The previous psychology and the woman's education and means, together with like circumstances, so act upon this class of disturbances that it is difficult to speak of them in generic terms. But we can indicate the most frequent. These *psychic causes* explain how anamolies of libido are prolonged sometimes up to an advanced age when the aptitude of the organism for sexual love has long been definitely extinguished.

¹⁷Valuable observations on this point may be found in Guyot: *Breviare de l'amour expérimental*. Paris, Barral's edition.

of past sensations. Probably all these factors intervene in the process. Cases have been described (Tait and Smith, cited by Kisch: *Op. cit.*, note (13), p. 19 of women who only after being castrated experienced the voluptuous sensation during cohabitation. Doubtless these were cases of psychic aberration.

One circumstance which may assist in the abnormal course which sexual psychology takes in some of these women, is *their tendency, unconscious perhaps, to live intensely a group of sensations which in the natural law of life, not always in harmony with instinct, should soon end.* To enjoy avidly those pleasures which are about to disappear is a frequent attitude in normal life. For example, the agreeable sensation of resting is intensified when the hours are short in which we may enjoy it, or the pleasure of staying in an agreeable place when the moment of leaving approaches. And perhaps the eternal prestige of sexual pleasure, so unlikely to be dimmed, is due precisely to its unalterable fugacity. The same thing can be observed pathologically in certain patients. For example young tuberculous persons, vaguely comprehending the shortness of their days, gather up indiscriminately every means of material pleasure which will shortly be impossible. We all know of cases of women of very amatory life, who, in the critical age, conceive particularly tumultuous passions. And there are also women of serene and monogamous sexual life who, on reaching this age and entering upon this organic and psychic situation, may be launched upon evil courses if, as is so frequently the case, they do not find their proper mates able to satisfy the demands of this amorous intensification.

Late Romantic Episodes

In regard to that true *sexual disharmony* which frequently upsets a life normal until then, let us note that it is more often a sentimental disharmony than one of real sexual conflict. Everyday life has given to the care of the home a prosaic tinge which suddenly appears dull to the woman whose emotions have become exquisitely sensitized through the climacteric. Her husband neglects or disdains her. He has satisfied his monogamous curiosity and, moreover, is distraught by the very fullness of his social activities. Then the woman, perhaps with a disinterest not felt in youth, seeks in the wide, eternally fascinating fields of adventure a new passion which will satisfy this uneasiness which she herself does not understand. In this psychologic explanation, the reflection of a definite neuroendocrine phase, we find the reason for the majority of those ruptures of conjugal

peace which frequently surprise women who until then have been apparently and even really happy. I believe that this "secondary or late love" is the rock on which the woman in the "dangerous age" so frequently stumbles.

This psychologic conflict has been much exploited in literature. In *La Crise*, the physician, whose perspicacity is certainly exceptional in one of his position, defines it well and rightly insists on the fact that it may occur early, when yet there is no thought of the climacteric according to the classic gynecologic concept.

"It is," he says, "a normal disease which may attack the best of women, as they reach the threshold of maturity. Such is the attraction of the evil fruit which Eve held for the first time in her hands. Thus the most honored woman may sense a desire not to be resigned to death without having tasted it."

But Elsie Lindtner's admirable letter to Professor Rothe in *L'Age Dangereux* is especially interesting for its exquisite and touching penetration. It is superior to anything with psychologic pretensions which I have read on the subject. In this letter she explains, as only a woman and one of that age could, to her husband, surprised and angered by the unexpected flight of his wife, the intimate psychologic process which impelled her to seek elsewhere satisfaction for her restlessness which had lain dormant and had now been awakened by her age and by an emotional cause.¹⁸

¹⁸Perhaps I should reproach myself for an excessive use of literary examples in this chapter. I have done so because I believe them as instructive as physician's descriptions. The literary artist gathers his impressions direct from reality, without the scientific prejudices which take out the human value in physician's observations. Here lies the error of those writers who "document themselves," writing their stories in scientific libraries, asylums or hospitals. They lose all the value of the record, a value which they might have held had the writers gathered without artificial technical intermediation from life itself. In present-day literature there are many examples of this, in drama, novels, and stories written after reading Freud whose extramedical dispersion has been, and I believe will be of more disastrous consequences for society and for psychiatry itself. Another point I do not believe justified is the idea, now very widespread among the people and which some practitioners ridicule, that the physician penetrates with special profundity into the spiritual privacy of suffering persons. To the physician the excessive contact with the material blunts his psychologic penetration. This phenomenon is especially patent among gynecologists, whose field is limited to the genital tract, yet contrary to what excitable adolescents believe, they are the least intimate, at least specifically, with woman. The heroine of *L'Age Dangereux*, so often cited, uses these exact words; "I have spoken with many famous gynecologists and I have admired their knowledge. But in my heart I laugh at their simplicity. They know how to cut open and sew up, like children with their dolls. But they go no farther than that." Probably, and also contrary to current belief, the same thing is true of priests. I have talked with some

Matronly Beauty. Increase of Masculine Solicitude

Another circumstance which should not be forgotten in explaining some such cases is *suggestion through masculine solicitude*, which not infrequently increases in these latter years. The preference which some men feel for women who are in full maturity is well known. Some women confess that it is in this age they obtain the maximum degree of sexual success.

Madame de Recamier, one of the most interesting examples of the power of feminine fascination, entered the apogee of her sway over men at thirty-six.¹⁹ I could cite many other such cases. In art, in painting and especially in sculpture exaggerated representations of the mature woman abound as a type of beauty. In literature, too, there are frequent eulogistic descriptions of this matronly beauty. Some of these, despite their elevated and moral pretensions, clearly reveal a turbulent hormonal state.²⁰

But it is unquestionable that for more than mere physical reasons, the mature woman may reach in this age the maximum of her attractive power spiritually. Woman as pure form, a delight to the senses, is perfect for only a little while, scarcely beyond nubility. Then to her charms other suggestions are added, of form, line or movement. These belong to the restricted esthetic field but they constitute in masculine desire the weightiest incentive, that which enters through the eye.

¹⁹See Herriot's book: *Madame Recamier et ses amis*. Paris, 1924. The life of this woman is presented with innumerable comments on sexual psychology, which I cannot go into here.

²⁰Because it is so typical and because of the moralistic aura of its author I quote a page of Michelet which he dedicates to the woman who has entered upon this decline. After eulogizing her moral and intellectual superiority and the grandeur of her destiny, he complains of the injustice whereby these women are adjudged old only because the face is a little faded, and adds, "If the face is faded, does that say that the flesh is less firm? In these cases not rarely is the body twenty-five while the face is forty. There are wrinkles around the eyes and on the cheeks, it is true. But usually, the knees and elbows previously angular, now show pretty dimples." These details observed with such complacency show clearly a sexual inclination in the author, one shared by so many men for the type of matronly beauty. Michelet when he wrote these lines was sixty years old.

who after hearing torrents of feminine sins had no substantial idea of woman. When a patient says to me, as frequently occurs, "I come to speak as to a confessor," it is a matter, invariably, of no importance. Sin like disease is something external and dense which does not allow us to see what lies behind in the privacy of the human soul, inaccessible to the professional eye, medical or clerical. Therefore we must turn to the great artists, who are supreme psychologists. I said not long since, where I do not recall, that we can study human sentiments in the comedies of Shakespeare much better than in the *Book of Passions* by Descartes. To have a complete picture we cannot get it all from books, but neither can it all be learned from life.

"Plastic beauty" is transformed into "sexual beauty." Finally, when the physiologic descent begins in the crisis, the feminine soul, matured so late, frequently offers this charming and intellectual complex, still impregnated with a sexual character reaching down to the instinct through cerebral routes, but which often enslaves the man more firmly than the attractions displayed in younger years.²¹

For all the aforesaid reasons this climacteric accentuation of sexual impulses occurs with some frequency. It may be limited to a subnormal psychic state or may reach frankly pathologic grades, either through its intensity or through its persistency until an advanced age. In the latter case it should be included among the psychopathies, such as erotism. These I shall discuss later.

²¹It would be interminable to cite the opinions of writers who, because, of the motives just explained, proclaim the excellence of the autumnal woman. The most interesting, doubtless, is that of the greatest master of love, Ovid. In his lines "Nec quotus annus eat nec quo sit nata require," (Ars Amatoria, Liber II) he states that the woman whose youth is past, including her whose hair is gray, is a good field for seeding. In this age he says, "women are particularly clever in love," adding the well-known demonstrative details which I have not copied here, and which are not attained until the thirty-fifth year; haec bona non prima tribuit natura juventae quae cito post septum lustra venire solent. Lord Byron (Don Juan, book X) also says that "the young woman ignores the elements and especially the nuances of love"; "in her maturity only does she comprehend what it is and what it requires." When Leonarda now autumnal, gave her age as an obstacle to the love of Augustus, almost a boy and passionately enamored of her, he answered her, "The years in passing have left more force and light in your spirit." (Björnstjerne Björnson, *Leonarda*.) Here is another more modern opinion: "What woman is the most beautiful? I believe that every delicate spirit prefers in woman this ripe hour of autumn when in her gracious physiognomy are mingled the echoes of the girl and uneasy anticipations of decrepitude. In this moment the woman is the synthesis of herself. She brings us in essence her past springtime even while she diffuses the rigor of future snows." (Ortega y Gasset. *Reconancias*. El Sol, April, 1919). The contrast between the first signs of physical decadence and the vigor of the instinct which divines it, especially in the glance, is doubtless a motive of sexual attraction. Probably the fashion of wearing white wigs which obtained in the eighteenth century, a vogue of wider acceptance than any of our modern fashions, was doubtless related to this same feeling. E. d'Ors, expresses this phenomenon admirably when he says: "Thou art now, Mercedes, in that moment of tempests and reefs wherein there gleams upon your temples the ashes from the live coals of your eyes": I find it a clinical fact parallel to this modality of libido under the circumstances, to which I have already referred and upon which I shall dilate later, that premature gray hair, far from being a sign of premature senility, coincides in a great majority of women with an energetic and lasting ovarian function. This might be the occasion for a long disquisition to demonstrate how the variations of the fashion almost always respond to motives related to the sexual instinct. For example, the sexual prestige of gray or white hair has come to be an advantage to the man, and in Chapter XXV I shall speak of how it corresponds to a modern modality of libido. Along with these and many other opinions favorable to feminine maturity which I might quote, I shall note a contrary one, that of Schopenhauer to the end that the man ceases to be attracted by the woman when she loses her conceptual aptitude. (Die Welt als Wille und Vorstellung. IV Auf., Leipzig, 1873.) This statement, wholly inexact, corresponds to his prejudice that the sexual instinct is a guide or selective agent, to bring forth a child in whom the good qualities of both parents are completed. This theory has entirely passed away scientifically.

Verbal Form of Hypersexualism

A special form of this climacteric hypersexualism which I have often observed is the following. In many women of irreproachable sexual honesty who, through social circumstances or religious ideals, have been kept from the slightest moral slip, this increase of climacteric libido is manifested by a thirst for risqué conversation or questionable jests, sometimes of an extremely erotic character. Yet such conversation or jokes they would have refused to give ear to formerly. But now they join in them with an assurance which they attribute to their age which authorizes anything. This sudden change may be very annoying to their intimates who are astonished at it. Unquestionably this is a verbal, compensatory form of the hypersexuality of the critical age.

Prolonged Youth and Internal Secretions

In closing let me note the fact that the retention of amorous feelings after the time when they normally terminate *is not an abnormal phenomenon in certain women. In these it is a perfectly physiologic fact corresponding to an abnormally conserved internal secretion of the ovary* or, in other words, a late climacteric. Along with their youthful feelings these women are apt to keep their beauty and premenopausal freshness which are so intimately linked to the internal secretions. I have seen two such cases of prolongation of youth and the conservation of physical beauty and amorous restlessness coincided with the continuation of menstruation up to the fifty-fifth and the fifty-sixth years. It would be interesting to have this detail in the case of Ninon de Lenelos, the prototype of this kind of woman, who married for the last time at seventy-five. At that age she still retained all the important elements of her beauty. In men the abnormal prolongation of physical youth and passion almost always coincides with an abnormal persistency of the internal genital secretion.

Tendency to Love Youths

An interesting aspect of these amorous feelings at abnormally advanced ages is *the frequency with which the individual who*

arouses them is of a younger age than the menopausal woman. This phenomenon is of common observation and has served as the theme for many novels in the last few years. It does not appear to be a question of an impoverished aberration in the biologic sense, but an instinctive tendency to seek in another's youth the warmth which her own waning power requires. From biblical times this way of struggling against old age has had a great reputation. When good King David was no longer able to combat the coldness of old age by usual means his counsellors advised this method. According to the legend the young virgin Abishag the Shunammite for several nights lay upon the royal couch and the desired end was achieved. No doubt this is the first record we have of ootherapeutic treatment. Many centuries later Hufeland²² raised this proceeding which men and women of all times and countries practice²³ to the level of a scientific system with the name *Geriatrics*.

Tendency to Sexual Inversion. Menopausal Virilism

The last psychic attitude of which I shall speak is the tendency to sexual inversion, *virilism*. I have spoken of the fact that *in certain cases in the climacteric, a heterosexual morphologic transformation occurs in the woman which is characterized by the appearance of certain masculine sexual signs, such as, general robustness, deep voice, down on the face and on the trunk.* I have also noted particularly that *the psychic state is altered likewise.*

²²Hufeland: *La macrobiotica*, Paris, 1838. As for this book, so often quoted in the last few years, it is not worth the effort of reading. Its author gives an impression of vulgarity which time does not dispel. An anecdotal resumé of the question may be found in Beauvois, *Essai sur la longévité humaine*. Un curieux moyen de prolonger la vie. *La gerocómica*. Neuvi. Iconographic de la Salpêtrière, 1901.

²³It is curious that in these loves between persons of different sex and of great difference in age, the sentiment is not rarely reciprocal. That is to say, the mature man or woman incline toward a young woman or a young man, perhaps for the reasons expressed. But, frequently, the younger person not only permits himself to be loved but really loves the one who is double his age. Many motives have a place in the second part of this phenomenon. I have seen some cases wherein the affection of a young man for a mature woman was engendered by a psychic state bordering on that which Freud called "the Edipus complex." That is, the men concerned had lived until then in an atmosphere of affection binding them to the mother. In one of my cases there was, moreover, a markedly appreciable physical likeness between the man's mother and the object of his affection. In the chapter on the masculine climacteric we shall see, on the other hand, that at present a social condition has retarded the "age of love" in the man and that under this influence many young women deliberately choose grey-haired lovers or husbands. There, too, we shall see that at times, the attraction of an older person toward a younger, has an implied homosexual feeling, an inclination toward the androgenous form near puberty.

The woman acquires an energy, sometimes an aggressiveness, which she did not have before and which approaches that of a man. The common people personify this transformation in the physical and psychic type of "the mother-in-law." To these characteristics there is added, less frequently, a change in libido. But let us note that the *two virilisms, the psychic and the somatic*, are not always joined. Cases are by no means rare of women who acquire a notably mannish caste of face while retaining all the psychic and emotional delicacy of strictest femininity, and vice versa. There are cases of "partial inversions" which I have studied with especial care. In considering the endocrine disturbances of the climacteric I shall speak of all this again.

It is now generally admitted, as I said before, that the inverse transformation of climacteric women is due simply to a revivification of the sexual expression of the opposite sex, more or less suppressed but latent in all individuals. This revivification is impelled by endocrine factors not yet well determined, but which may perhaps be due to the suprarenal cortex.

CHAPTER XVI

PSYCHIC SYMPTOMS. (C) CLIMACTERIC PSYCHOPATHIES

Outline

We shall study separately, as I have already said, first the *psychopathies* properly so-called, manias, melancholia, manic depressive states, and then the classic *neuroses*, neurasthenia, hysterism and epilepsy.

Frequency of Climacteric Psychopathies

Psychopathies properly speaking are extremely diverse in the critical age. I have said that their distinction from psychic states which are truly climacteric, as described in the last chapter, is very difficult. Some are the continuation of the latter without any sharp line of separation. Therefore, there is nothing more important to add save brief comment.

They are relatively infrequent. Statistics vary widely because of the difficulty of distinguishing between exaggerated, abnormal states like those just described and true psychopathies. But I believe that they really are rare because the cases I have seen are not numerous, compared to the number of menopausal women.

Rôle of Nervous Predisposition

One important fact on which all writers insist but Schickele¹ especially, and I too, repeatedly, is that *menopausal psychopathies appear in women only with markedly morbid nervous predispositions*. Or these women have had periods of frank dementia, often at sexual crises, puberty, menstruation, and pregnancy. Or they have had merely suspicious psychic peculiarities where the familial antecedents have not been openly neuropathic.

¹Schickele: Op. cit., note (14), page 19.

Usual Psychopathies in the Critical Age and Their Chronology

Here I would advance the opinion that there is no clinical peculiarity in the psychoses, properly so-called, of the critical age. They are like those which are presented in any other period of life. This explains the brevity of consideration accorded them by such psychiatrists as Kraepelin and Bleuler. The statistics of Tilt, Matusch and Kraft-Ebbing, which I do not copy because the terminology does not fit that of the present,² agree in giving *melancholia* and *paranoia* as the most frequent psychoses in this age. Schickele adds *manic depressive states*. It is interesting to note that these three psychopathic states are precisely those which are most frequent in hyperthyroidism, according to Sattler,³ Parhon,⁴ Rogers,⁵ and others.⁶ I shall comment upon the significance of this fact.

Sometimes the climacteric psychopathies are presented periodically, coinciding with the days of the menses which may still be occurring or may have ceased. Again this periodicity is not observed. But, in general, as Norris⁷ states, and I have repeatedly confirmed, they are apt to precede the true menstrual disturbances by a considerable period of time.

Most Frequent Paranoias in the Menopause

As special clinical types within the group of the paranoias I shall cite states of erotism, prolongation of the disturbances of sexual feeling, previously studied, which lead some women to lamentable extremes. Then frequent cases of *exhibitionism* appear, generally directed toward one certain man, or at times to

²Kraft-Ebbing observed among 60 cases of menopausal psychoses 4 melancholias, 1 circulatory insanity, 1 acute delirium, 42 acute forms and 12 paralytic dementias. (Traité clinique de psychiatrie, Paris, 1897.)

³Sattler: Die Basedowsche Krankheit, Leipzig, 1908.

⁴(a) Parhon: Op. cit., note (10), page 196.

(b) Parhon: Sur un cas de melancholie avec hypertrophie thyroïdienne succédant à la ménopause. Revue Neurologique, 1906, No. 14.

(c) Parhon and Marie: Contribution à l'étude des troubles mentaux de la maladie de Basedow, L'Encephale, 1906, No. 15.

⁵Rogers: Antithyroidine, New York Med. Rec., 1912, No. 14.

⁶Bleuler: Tratando de Psiquiatria, Spanish edition of the fourth German edition, by Villaverde, Madrid, Calpe, 1924, also cites, between the psychoses of hyperthyroidism, and on the side of manic depressive states, certain "pseudocatatonic forms," difficult to differentiate from true catatonias. My wide experience with this disease is in frank disagreement with that of Bleuler, owing no doubt to differences in the national character. I have never seen these pseudocatatonias.

⁷Norris: Op. cit., note (13), page 104.

men in general. Gueneau de Mussy's study of the *erotism of the menopause* is classic.⁸ The pathologic exaltation of the amorous instinct may take on a *platonic character*, chiefly in unmarried menopausal women. They fall in love with a man whom they believe responds, interpreting his indifferent acts, a glance, a phrase, a casual meeting, as proofs of love. This rather frequent type has been exploited numberless times by comic writers.⁹

Religious delirium, or mysticism which develops in many women, especially in Spain, come within the group of exaggerated feelings but are outside the pathologic group of the type of *la beata* [the blessed, a religious order in Spain]. As I have said a great number of menopausal women turn to this order. These have lost, or are about to lose, the elements of sexual success and with archaic ardor they enter mysticism as a last spiritual refuge wherein they always find a congenial atmosphere which is also suggestive. The critical age is the time of profuse gifts to the church, of establishing foundations with which the donor hopes to buy pardon for the past and the guarantee of eternal salvation. Much rarer are the cases of true religious insanity with *visual, auditory, tactile* and other *hallucinations*, sometimes mingled with erotic sensations. A multitude of these cases has been described. I have seen others wherein the mystic delirium was focused upon a person who is connected with the cult, as a priest, whom the woman makes the object of her platonic effusions.

Many cases exhibiting *morbid envy, dysomania, kleptomania* and like traits, have been described.¹⁰

Melancholia. Involutional Melancholia

As I have said, *melancholia* is also frequently presented, in the critical age, in all its forms so well known to psychiatrists. There has been an attempt to make out a special type belonging to this age, with the name of *involutional melancholia* (Kraepelin) or *presenile melancholia*. Under both names it has been much discussed and I shall add a few comments.

⁸Gueneau de Mussy: *L'erotisme de la menopause*. Gaz. hebdomadaire, 1871.

⁹The comedy by Arniches *La señorita de Trévelez* gives ample evidence of acute psychologic observation of this kind of climacteric disturbance.

¹⁰See a recent case reported by Laignel-Lavastine: *Manie raisonnée hypochondriaque post-menopauséique avec caféisme*, Soc. de Psychiatrie, October, 1921.

The appearance of the melancholia of involution is preceded by a prodromal period, generally very long, characterized by diverse vague disturbances of different organic activities such as anorexia, painful digestion, insomnia, irritability, pessimism and tendency to rapid fatigue. But according to my experience in other cases the melancholic state comes on most suddenly. In one way or another the disease is established, being characterized from its beginning by intense psychic suffering, extreme emotionalism and various disturbances of physical order such as tachycardia, palpitation, sensation of respiratory oppression, deep sighs, anorexia, dyspepsia of various types such as hypochlorhydria, hyperchlorhydria or alternations between the two. In others we find the symptomatology of flatulent dyspepsia predominating, constipation, emaciation, with more or less marked changes in the composition of the urine, principally a diminution of urea. Migraine, tremors, insomnia, hysteriform attacks are also seen. Besides this marked form of the process, there is a whole series of attenuated types whose description would be interminable.

Often the involutional melancholia is associated with states of anxiety, constituting *anxious melancholia*. The anxiety may be followed by agitation, *agitative melancholia*, or by stupor which on occasion is most intense. There may be mental confusion, almost always transitory, but in the majority of cases there is perfect lucidity. In every way psychic disturbance properly speaking offers a great variety of types, which establish an insensible gradation from the lightest and most transitory forms of involutional melancholia to manic depressive dementia.

Manic Depressive States, Their Relation to Involutional Melancholia

This is, as I have indicated, the third of the varieties which form the greater portion of dementias in the menopause. They are presented under all their clinical types, which it would be out of place to describe here, from mild *cyclothymias* up to intense manic depressive processes. They are always characterized either by excitation, flow of ideas and words, and a motor and vegetative *exaltation* which we shall see presently exactly

reproduces that appearing in Basedow's disease; or, through psychic inhibition, by depression and anxiety. These phases appear either singly or alternately.

I shall dwell only on the clinical relation which one of these manic depressive states has to the involutional melancholia, described above. Dreyfus¹¹ has pointed out this relation and Kraepelin¹² accepts it. Now there is a certain unity in the majority of these cases of emotional melancholia presented in the menopause. Hence, even writers who like Bleuler deny, perhaps rightly, that there is any clinical individuality to *involutional melancholia*, nevertheless admit that "in the period of involution there are presented preferably certain forms of depression and anxious states, and perhaps certain psychoses only occur in this age."¹³

Involutional Melancholia and Arteriosclerotic Psychoses

The fact is, that there are presented with some frequency in the climacteric, melancholic and manic depressive states which because of their chronology and their strongly marked emotion have a certain clinical individuality, although their exact nosologic limits are not very clear. Their relation to the arteriosclerotic and senile dementias is, indeed, so close that in many cases it is only toward the end that they can be distinguished. Both appear in the same age. Their symptomatology is similar, and objective examination which might reveal such signs as arteriosclerosis is not apt to be very decisive. They differ in that involutional melancholia is apt to pass away when the genital crisis is over, whereas the senile and arteriosclerotic psychoses increase progressively. But this does not give absolute assurance against the return of the trouble. I have seen cases wherein after a longer or shorter period of recovery the disease reappeared in definite form and with the characteristics of arteriosclerotic dementia. For this reason Kraepelin's criterion seems proper, to include all these states under the common name of "psychoses of decadence."¹⁴

¹¹Dreyfus: *Die Melancholie, ein Zustandsbild des manisch depressiven Irrenseins*. Jena, 1907.

¹²Kraepelin: *Psychiatrie*, Leipzig, 1910, ed. 8, vol. ii.

¹³Bleuler: *Op. cit.*, note (6), page 218.

¹⁴This translation ("psicosis de la decadencia,") proposed by Villaverde of Kraepelin's term "Alterspsychosen" appears correct to me.

Thus, then, the physician ought to be very reserved in the prognosis of these melancholias and manic depressive psychoses of the involutional epoch.¹⁵

Even in those cases wherein the psychopathic episode has definitely disappeared my experience teaches that the individual is not likely to remain entirely normal but retains a certain sub-normal depression or excitation, with excessive *emotionalism* or with a more or less ostensible lowering of her intellectual capacity.

Suicide in the Critical Age

Within the special symptomatology of the various psychoses described as occurring in the menopause *the tendency to suicide* is marked. This has been pointed out by Squirol. He observed that of 198 female suicides, 77 were from forty to fifty years old, and were, therefore, in the midst of the menopausal crisis. Here is one of my cases, which is interesting because of the absence of other definite psychic symptoms.

CASE 49.—S. de L. Woman of forty-one years, married, no children, very tranquil life, very religious. She had lived *happily* in her calm surroundings, and she shocked her relatives and all who knew her by her suicide which she accomplished by drinking poison. She left no note which would permit conjecture as to the cause of her act. Nor had the most intimate of her relatives and friends heard, in the days just preceding the tragedy, the slightest word which would indicate the grave crisis through which her spirit was passing. There was *perhaps only a slight accentuation of her usual state of mind which was always a little sad but still well within normal limits*. Yet it was known that *menstruation*, never very active, *had been absent two months*. This, together with her sterility and her tendency to obesity permits the supposition that she had a certain ovarian insufficiency with a premature climacteric, to which the suicide might properly be related.

¹⁵We find ourselves here in the same position as we were when considering the other phenomena coincident with the climacteric, for example, arterial hypertension. Is it a functional upset? Is it an early phase of a state of vascular sclerosis? Are they two distinct states which succeed each other?

General Paralysis and Climacteric

Let me recall a curious fact. For some time the menopause was considered by Sepelli,¹⁶ and others, as the cause of a *paralytic dementia* or *general paralysis*. Now we know that this disease has a specific etiology well recognized. But perhaps the endocrine disturbance of the climacteric with its train of circulatory and nervous phenomena of nervous type may cause some of the symptoms seen in this disease.

Pathogeny of Climacteric Psychopathies. Hyperthyroidism

All psychiatric pathogeny is more or less obscure; hence absolute clarity is impossible in this climacteric sector. We must keep in mind, however, these three facts: (1) *the previous mental constitution of the subject decisively influences the behavior of the nervous system at the time of the crisis*. The latter only throws into relief latent psychopathies or temperaments of greatly marked psychopathic tendency. As the majority of present-day psychiatrists now admit, these latent tendencies correspond respectively to the usual forms of psychoses. (2) It must never be forgotten *that the critical age is the age of the onset of arterial lesions especially in subjects who are predisposed either through inheritance or acquired conditions, such as syphilis*. These lesions are important in the genesis of psychopathies. (3) *In this age important humoral, endocrine factors enter into play. The influence of these upon psychic function is unquestionable and merit some comment*.

In the previous chapter I spoke at length on the influence of the *internal genital secretions* on psychic function and need not repeat it here. But in the climacteric crisis there are other important coadjuvant factors, especially *hyperthyroidism*. The direct action of this last upon psychopathic states is now recognized by all modern psychiatrists including those who, like Bleuler, are rather more stubborn about admitting this kind of humoral influence in the pathogenesis of the mind.

Culbertson,¹⁷ looking from the other point of view, the endo-

¹⁶Sepelli: *Paralysie générale chez la femme*. *Annales med. de Psychiatr.*, 1884; see also Icard, *op. cit.*, note (18a), page 108, who states that "there are numerous writers who say that ordinary menopause is the cause of paralytic dementia."

¹⁷Culbertson: *Op. cit.*, note (28), page 21.

ocrine, attributes a predominant rôle to hyperthyroidism in the determination of the psychic symptoms of the menopause. Indeed of all the endocrine elements which make up the climacteric crisis, hyperthyroidism is the one most frequently accompanied by psychic manifestations and these are *precisely*, as I have indicated, the same as those seen with greater frequency in the critical age. Moreover, I have observed clinically a greater intensity of the climacteric symptoms of hyperthyroid, and perhaps hypothyroid-adrenal, background in menopausal women with psychopathies. These intensified symptoms were tachycardia, changes in weight, tremor, severe vasomotor disturbances and so forth. In fact, different writers have recently studied the unquestionable relation existing between manic depressive insanity and hyperthyroidism. Kahn,¹⁸ Parhon,¹⁹ and Lafora²⁰ call attention to these three essential points which I have indicated in this chapter: (1) In the symptomatology of manic depressive dementias there are many symptoms of hyperthyroid origin. (2) In hyperthyroidism with psychic anomalies the most frequent disturbance is the manic depressive psychosis. Bleuler says "it is rarely lacking." (3) Antithyroid remedies, such as antithyroid serum, bel-ladonna, etc., may effect excellent results in certain manic depressive states. An argument still more in favor of this relation is the one I just brought forward, namely, the coincidence of manic depressive psychoses in the menopause with marked hyperthyroid reaction. Rosenfeld²¹ orients his recent views from this same direction. He concedes an extraordinary importance in manic depressive states in general to vasomotor disturbances. Let us note only that these disturbances form an essential part of the symptomatology of the climacteric age and that hyperthyroidism intervenes prominently in its pathogenesis.

Prognosis of the Mental Disturbances of the Critical Age

The *prognosis* of climacteric psychopathies is more benign in some types than for psychopathies in other periods. This is due to the limited duration of the greater part of the symptoms of

¹⁸Kahn: *La cyclothimie*, Thèse de Paris, 1900.

¹⁹Parhon and collaborators: See bibliography on page 218.

²⁰Lafora: *Op. cit.*, note (14), page 196.

²¹Rosenfeld: *Arch. f. Psychiatrie*, xlv (cit. by Schickele *op. cit.*, note (14), page 19).

this state. Attention has been insistently called to the error into which such a rule would lead us, because of the possible presence of presenile lesions in the nerve centers. In fact I do not believe general rules can be laid down on this point. The prognosis of each psychopathic type will be different. That is, the prognosis of melancholia or paranoia will be modified in each instance by individual circumstances, such as the intensity of the circulatory phenomena and the personal and hereditary antecedents. It is evident that the mild psychic manifestations, emotionalism or disturbances of sexual feeling, which we have studied as directly dependent on the sexual upset are likely to be transitory. This fact has no doubt contributed to the idea, not wholly correct, that true climacteric insanities are mild in character.

With all of these reservations we may consider *involutional melancholia* as the most characteristic psychosis of the critical age. According to Rogues de Fursac and Rosanoff²² its prognosis may be set down as follows: The disease ends in *complete recovery* in 66 per cent of cases. It ends by transformation into definite states of dementia, dependent on cerebral sclerosis in 8 per cent, and in death in 25 per cent. Fatal termination is due to three causes in this order of frequency—suicide, excessive melancholia through intensity of depression, defects in alimentation, digestion and nutrition, and various complications not of the nervous system such as pneumonia, influenza and tuberculosis.

Influence of the Climacteric on Preexistent Psychopathic States

Another interesting point in *prognosis is the influence of the menopause on preexistent psychopathic states*. There is a current belief that this influence is beneficial. Such an idea has arisen through the common observation that women suffering from this kind of disturbance recover after the disappearance of the menses. Some old writers like Merson even affirmed that 47 to 59 per cent of psychoses are cured in the menopause. Griesinger is of the same opinion. On the other hand Kowalenski and Matusch have observed this improvement only in some cases.²³

We need precise data on these statistics as to the nature of the

²²Rogues de Fursac and Rosanoff: *Manual of Psychiatry*, New York, 1918.

²³Kisch's citations: *Op. cit.*, note (13), page 19.

psychopathic troubles which were included. Very likely neurotic processes, neurastheniform and hysteric states figure in them and these, as we shall see presently, may greatly diminish in severity, or even disappear, after the critical age. Undoubtedly some cases of true psychosis are improved in the menopause, or are at least favorably modified in that they are corrected from states of excitation into more tolerable apathetic ones (Matusch). *But in general the influence of the climacteric crisis on mental abnormalities appears to be prejudicial*, because the very pathogenic conditions favor psychic disequilibrium, as we have seen, and because the approach of senility notoriously prejudices mental function.

Neurosis and Climacteric. Hysteria

I shall add a few words on the neuroses which play so great a rôle in different incidents of genital life and, consequently, in the critical age. This is a matter of common observation from the time of Balzac.²⁴ Of this group we shall consider *hysteria*, *neurasthenia* and *epilepsy*.

The close relation existing between *hysteria* and genital disturbance has been known from ancient times. Formerly the trouble was related to the uterus. Now we know it depends upon the internal secretion of the ovary. This purely anatomic fact has acquired a psychologic vogue in the last few years which has become widely known through Freud's studies. These demonstrate the rôle of libido and its disturbances in the genesis of neurosis.²⁵

Experience teaches us, in fact, that puberty, menstruation, the various diseases of the genital organs and disturbances in the sexual and amatory sphere, which in turn react on ovarian endocrine function, powerfully influence the course of hysteric symptoms. *How much greater must be the effect of the climacteric because of the decrease in emotional control occurring in this age,*

²⁴Balzac: *Physiologie de l'amour*, Paris, 1890. Read the exquisite chapters devoted to the study of migraine and neurosis.

²⁵I have already cited Freud's fundamental bibliography, note (7), page 193. I insist that Freud does not realize the relation between his psychic parallel to them.

for emotion plays a great part in the symptomatology of hysteria in all sexual crises, normal or pathologic.

As a pathologic concept hysterism soon evolves into a form which we cannot take up here. Like that of the neuroses in general its course is limited. But there remains a clinical group of patients with a definite mentality and psychology which well corresponds to the concept of hysteric neurosis. *Upon this neurosis, now constitutional, the climacteric episode acts like any other such episode, only with greater intensity perhaps.* Just what the effect will be in a given case depends on many unforeseen circumstances. In general terms they may be summarized thus: *The excitation phase of neuroendocrine instability, through which most women pass in the first stages of the climacteric, acts unfavorably on hysteria. On the other hand, when definite suppression of the ovary, and of the whole neuroendocrine system in general, occurs, the symptoms lessen and even disappear.* Thus we may explain the different types of hysteric reaction in the climacteric which have been described by writers. Here is a typical case of hysteria which was aggravated in the early stages of the crisis and later cured.

CASE 50.—N. R. Always hysteric with severe typical manifestations throughout life, exacerbated by an abnormal sexual life; menses normal. Usual mentality definitely hysteric. An aggravation of all her symptoms at the forty-second year coincided with hypertension, sensations of heat and other menopausal manifestations. A year later menstrual irregularities occurred. Later they ceased. Then the *hysteric phenomena were intensified extraordinarily*; attacks, oppressions and varying paralyses, sometimes in an eyelid or an arm; pharyngeal constriction which lasted several days; digestion was impaired; hysteric psychology greatly exaggerated. This turbulent period lasted two years. Then, parallel to the subsidence of the menopausal crisis, a *progressive lessening of the hysteria began*. Now five months have passed without menses and the hysteria clinically has completely disappeared.

A very notable case of recovery from a stuporous form of hysteria on the cessation of sexual activity is that of the celebrated

sleeper of Okno, whose clinical history is given by Froederstrom.²⁶ This woman slept from her fourteenth to her forty-sixth year; that is, during the whole period of sexual activity. Recovery coincided with the definite cessation of the menses. In general, old stubborn cases of hysteria which are modified for the better by the menopause are not rare, whether the crisis be chronologically physiologic or early as in the following case.

CASE 51.—S. O. Thirty-six years old. Infantile type. Tendency to obesity. Menses always scanty. Married. An only child. In short, *congenital ovarian insufficiency*. Two years ago the menses became more scanty and infrequent. This was accompanied by different vasomotor and nervous phenomena which were relieved by ovarian extract. A year later a *pseudocomatose attack occurred which lasted several days*, leading one to think of uremia, encephalitis or meningitis. But proper examination did not confirm any of these hypotheses. *In the following ten months the menses did not appear and an obvious improvement in the nervous disturbances coincided with the amenorrhea.*

An equally favorable result has been observed in some hysteric patients following castration performed because of various genital infections. I have seen three very typical examples. In general the younger the patient the more immediate is this action of castration on hysteria. That is, the farther the woman is from the age of spontaneous menopause the quicker the result. This is easily explained if we keep in mind that surgical ablation of the ovaries causes hardly any secondary neuroglandular reactions in young women, while it does cause intense reactions in proportion as the woman's age approaches that of the critical. In early castration the lack of the ovaries and the lack of excitant reactions favor sedation of the hysteric phenomenon. In late castration, although the ovary is lacking, the neuroglandular instability evidently prejudices the nervous system.

[I have attempted an explanation of this well-recognized fact

²⁶Froederstrom: La dormeuse d'Okno, 32 ans de stupeur. Guérison complète. Nouv. Iconographie de la Salpêtrière 1912. I published (op. cit., note (19), page 124) a case of accessional pathologic sleep in a woman who had symptoms of thyroid insufficiency. The sleeping attacks, which had all the clinical characteristics of hysteric phenomena, were alleviated on treating her thyroid insufficiency. There was always a doubt as to what part psychotherapy might have had in this relief because she was a woman who acquired, in a Swiss sanitarium, suggestive and fantastic notions regarding the action of the internal secretions. At the forty-fourth year the menses ceased and so far she has had no more sleeping attacks.

relative to the milder menopausal reaction occurring in young women. It was suggested that this reaction depends in some way on the length of time the ovary is associated functionally with the other endocrine organs. The shorter this "duration of association" is, the milder the reaction upon ablation of the ovaries.—C. C.]

The coincidence of recovery from this neurosis upon castration was so recognized that *for many years surgical treatment by oöphorectomy was widely proclaimed for hysteria*.²⁷ Later the influence which suggestion had in some of these cases was stressed (Pitres²⁸); also the fact that, in some cases, castration was effective because through it such lesions as inflammatory conditions and cysts were removed and it was these which really caused the hysteria.

Cases have also been cited wherein hysterism appeared for the first time in the physiologic menopause, in women who had been healthy until then (Axenfeld, Brachet, cited by Vinay²⁹), *or after an early menopause* (Alaize), *or even following castration*. Clearly in these cases we cannot interpret the climacteric crisis as in any way producing the hysteria. Here it acts only as an "occasional cause," or it merely reveals a previous latent state, granting the correctness of the diagnoses made by these writers. We must be very cautious in accepting retrospective diagnoses of hysteria.

Neurasthenia and the Critical Age

The concept of *neurasthenia* is also undergoing a rapid change being worn down on all sides. Part of the cases which have been diagnosed classically as neurasthenia now pass over to be incorporated in other well-defined diseases, like hysteria, melancholic states, or those of schizophrenia, or initial paralysis. It is certain that neurasthenia as a syndrome produced by an excessive mental fatigue, without original psychopathic elements and therefore yielding to a simple treatment of rest, is a relatively rare disease. But in practice neurasthenia such as Bard describes, leaving out incorrectly diagnosed cases, includes a great number of patients who are neither ill from overwork nor can they be put

²⁷See the bibliography on this question, besides the general works given, in Alaize' thesis: note (8), page 19.

²⁸Pitres: *Leçons cliniques sur l'hysterie*, 1891.

²⁹Vinay: *Op. cit.*, note (12), page 19.

into any of the well-known psychiatric pigeonholes. Yet when we try to get away from this vague concept of "neurasthenia," we come upon the still vaguer term "pseudoneurasthenia" which Bleuler uses.³⁰

Thus while the term neurasthenia is transitory, it continues useful and at times cannot be replaced by any other, as is true also of the term arthritis. The psychiatrist who in his lectures and writings severely condemns the abuse of the diagnosis "neurasthenia" will surely find himself obliged, in spite of everything, to be prodigal with this term in his own clinic.

My experience along this line is not to be despised since, as Bleuler says, the general practitioner sees more neurasthenics than the neurologists and many more than the psychiatrists. *My opinion is that it is precisely in this age that the most frequent and authentic cases of neurasthenia appear, especially in men*, as we shall see in Chapter XXV. Of course it is plain that physical or mental work, no matter how intense or continued it may be, does not give rise to neurasthenic states if the brain be normal. At the most, transient weariness occurs which does not require medical treatment. But when an unstable nervous system is concerned and when, upon much or little work, depressing emotional attacks of various kinds have persistently appeared, a nervous collapse may occur, the *run-down* condition, in the American phrase. This collapse will bear the symptomatology of classic neurasthenia including ultimate recovery. This state, I repeat, occurs with great frequency in the climacteric which is the period, let me say it again, of greater sensitiveness, of more emotional attacks, and above all the period in which there comes a breaking down of the desire to live which is so linked to the sexual instinct.

But let us not forget that this is also the period propitious to melancholic states, arteriosclerotic psychoses and like conditions, whose beginning may be clinically identical with a simple neurasthenia.

Epilepsy and Climacteric

The contributions of those who insist upon the relation of epilepsy to different endocrine disturbances are numerous and well-known. Every variety of opinion is offered, from that of

³⁰Bleuler: *Op. cit.*, note (6), page 218.

those who, like Buscaino,³¹ made this syndrome dependent upon a thyroid disturbance, down to that of recent neurologists who, since the period of "antiendocrine reaction" aroused by Gley, contemptuously and decisively deny any such relation. Still many scientific men merely follow along, without entering the lists to propose or defend any theory bearing on this subject. Such an attitude is the least excusable of all, for to venture forth upon the road of an unsound hypothesis is as contrary to the deliberate behavior of the true scientist as is the disdaining, through mere prejudice, of the priceless facts offered by the clinic. *So great is the coincidence of epilepsy with various endocrine diseases and symptoms that it merits an attempt at interpretation which goes farther than considering this coincidence merely casual.*³²

In my other text³³ I summed up my opinion and I now ratify it here.

"In my opinion there are three points of contact existing between the two processes, epilepsy and endocrinopathies. It is very probable that in many cases *the same etiologic factor gave rise at the same time to the epileptic and the endocrinopathic states*, as for example, syphilis, especially if hereditary, which plays such an unquestionable rôle in the pathogenesis of epilepsy and also in many diseases of the glands of internal secretion. Castex and his school have conscientiously exhausted this last

³¹Buscaino: Ricerche sul significato biologico delle alterazione qualitative della tiroide. Riv. di patol. nerviosa e mentale, xx, 1915.

³²Among the articles on the relationship between epilepsy and the endocrine glands, I may mention:

(a) Van den Berg: Epilepsy Suggestive of Endocrine Relationship, Endocrinology, 1921, p. 441.

(b) Sanchis Banús: Estado actual de la cuestion de la epilepsia. Archivos de Medicina. Cirugia y Especialidades, 1921, No. 13. Revista general con alusiones ciertas a la teoria endocrina.

(c) Marchand: Glandes endocrines et epilepsie. Rev. Neurologique, 1922, No. 12. The list of references given in this article is very complete but the author is timid in his criticism. It is from this monograph that I have taken many references given in this chapter.

(d) French: Epilepsy and the Endocrines, Am. Jour. Clin. Med., October, 1922. This refers principally to the thyroid and parathyroid disturbances.

(e) Rebathu, Mallon et Sedaillon: Epilepsie et fonctions ovariennes. Soc. Méd. des Hop. de Lyon, June, 1922.

(f) Kern: The Rôle of Endocrinology in Epilepsy, Am. Jour. Clin. Med., September, 1923. He supports a pluriglandular theory.

(g) Juarros: Los organenes de la epilepsia genuina. Siglo Médico June, 1924. General review with bibliographic allusions and comments on the endocrine theory.

(h) See also Pende's work (op. cit., note (17), page 19, which contains bibliographic data and a critical summary which in its essential points coincides with mine.

³³Marañón: Op. cit., note (11), page 54.

point." Again, "*endocrine elements may enter into the pathogenesis of the degenerative states which constitute the epileptic predisposition.* Thus these patients often present such symptoms as a thyroid hypertrophy, functional thyroid reaction, disturbances of growth or pigmentation. Finally, it is certain that, *in subjects with a latent epileptic predisposition, epilepsy may accidentally arise through an incidental cause, such as an acute hyperthyroid attack, hypophyseal disease, or the complex crisis of an abnormal menopause.*"

These general principles can be applied in the concrete case of the menopause. *In some cases of latent epilepsy the climacteric incident may give rise to convulsive attacks for the first time.* In the first edition of this volume I stated that "the age in which the climacteric occurs is not favorable to the appearance of epilepsy." But Sanchís Banús' basic work,³⁴ which came out a short time later, and some new observations of my own, have compelled me to correct this statement. As Sanchís Banús indicates, *I do not consider the climacteric as more than a determining cause of the attacks, which therefore develop in those women who have a previous latent epileptic constitution.*

To the cases collected by Sanchís Banús I add the following:

CASE 52.—J. Q. Forty-four years old. Always healthy. No epileptic, neuropathic, syphilitic or other antecedents. Married. Several normal deliveries. The first menstrual disturbances appeared at the forty-first year. *Coinciding with these, typical epileptic seizures occurred, approximately each month and almost always in relation to the menstrual episode.* Negative Wassermann reaction. Urine normal. Tension 19-7.

CASE 53.—S. Ch. Forty-eight years old. Married. Multipara. No important antecedents such as psychopathies or neuroses. A mild suspicion of congenital syphilis but the Wassermann reaction was repeatedly negative. *Six years ago the first retardation of the menses occurred. Since then typical, nocturnal, epileptic seizures.* Constipated. Urine normal. Tension, 14-9.

CASE 54.—C. O. Sixty-two years old. Always very "nervous," but without anything of systemic importance. No suspicion of

³⁴Sanchís Banús: Epilepsia climáctica, Archivos de Neurologia, 1920, No. 3.

syphilis. Multipara. The menses suddenly ceased at the fifty-second year, *and on the first day they were missing she had the first attack, typically epileptic.* The periods returned, but with great irregularity until they finally ceased altogether. The attacks persisted with an approximately menstrual rhythm. Urine and Wassermann negative. Tension 19-10. Much improved under bromides, ovarian extract and diet.

CASE 55.—M. D. Fifty years old. Unmarried. The periods ceased at the forty-second year. *Coincident with the menstrual disturbance the first epileptic seizure occurred.* The attacks were repeated, being sometimes typical or again taking the form of prolonged dizziness, continuing to the present time. I saw several attacks. No antecedents. Wassermann reaction negative. Urine normal. Tension 22-9. Arteriosclerotic signs were beginning. Two years later nocturnal hemiplegia, probably during a seizure. Death some months later.

Thus, undoubtedly, there are cases of epilepsy wherein the attacks may appear on the occasion of the climacteric disturbance. Note that I say the attacks may so occur, not epilepsy. If this distinction be borne in mind there is no harm in speaking of "*climacteric epilepsies*" when no greater importance is given the adjective than is given in the expressions "early epilepsies," "late epilepsies," "arteriosclerotic epilepsies," "emotional epilepsies," "digestive epilepsies," and many others wherewith no pretense is made of clearing up the pathogenetic mystery of the disease. Such expressions are used merely to group cases about a clinical fact, or perhaps about a therapeutic criterion.

Probably the climacteric has an influence through the metabolic modifications and the changes in arterial pressure, which are sometimes produced through the ovarian insufficiency itself, sometimes through the glandular reactions which accompany it. The variety of these reactions explains why the attacks seem to be produced through surgical suppression of the sex glands,³⁵ while at other

³⁵(a) Marchand: *Epilepsie convulsive survenue apres une ovariectomie.* Revue de Psychiatrie. September, 1899.

(b) Marchand: *Influence de l'ovariectomie sur l'epilepsie.* Soc. Med. Psychol., June, 1920.

(c) Cases reported by Torre Blanco and Jiménez Diaz, cited by Banús; Note (34), page 232.

(d) Wallan: cited by Marchand; Op. cit., note (32c), page 231.

times the operation brings relief.³⁶ For the latter reason this operation has been recommended in the treatment of epilepsy.³⁷ A similar glandular disturbance may, indeed, produce contrary results. Keep in mind that it is not a question of the presence or lack of a specific hormone, but of a diffuse, general action which is humoral and circulatory whose influence may be beneficent or pernicious, according to the particular case. We find many such examples of this. Thus, the same excessive use of bromides may cause a state of gastric hyperacidity or a catarrh with hypochlorhydria. Ovariectomy may cure osteomalacia or produce it. In epilepsy, menstruation may alleviate the attacks or coincide with them. But all in all *the burden of data is on the side of ovarian insufficiency as being rather a provocative element in the attacks*. Besides the cases reported by Sanchís Banús and by myself of attacks which began in the climacteric, similar ones have been given by Marchand³⁸ and by Perrin and Richard.³⁹ Toulouse and Marchand⁴⁰ cite cases of improvement in the attacks during pregnancy. This fact should, in my judgment, be attributed to the excess of luteal function occurring during almost the whole period. Ashe⁴¹ reports patients in whom youthful ovarian insufficiency coincided with the beginning of the attacks. Marchand has found that the graafian follicles are less abundant in epileptic than in normal women, rarely having attained their complete development, and in two cases they were wholly absent with, moreover, a "sclerosis of the medullar layer."⁴²

³⁶See a very typical case selected by Ventra; *Sindromi epilettiche di natura endocrina*. Il Manicomio, No. 2, 1924.

³⁷(a) Bacon: *Emploi de la castration dans le traitement de l'épilepsie*, Arch. de Neurologie, 1880.

(b) Levi Bianchi: *Les épilepsies menstruelles, etc. L'ovariotomie proposée comme traitement radical des épilepsies menstruelles*, Il Manicomio. No. 1-2, 1909.

(c) Schvan: *Ovaries and Epilepsy*, Med. Rec., February, 1887.

(d) Russell, cited by Marchand, op. cit., note (32c), page 231. From all these should be eliminated possible cases of false epilepsy, hysteria, etc.

³⁸Marchand: Op. cit., note (35), page 233.

³⁹Perrin and Richard: *Troubles endocriniens et épilepsie tardive*. Rev. Neurolog., 1919, p. 698.

⁴⁰Toulouse and Marchand: *Influence de la menstruation sur l'épilepsie*, Revue de Psychol., May, 1913.

⁴¹Ashe: *Ovarian Insufficiency as a Probable Cause of Epilepsy*. Dublin Jour. of Med. Sc., May, 1919.

⁴²I cannot understand how Marchand passes scornfully over anatomopathologic data like these, the significance of which in respect to glandular insufficiency is indubitable.

Claude and Schmiergeld⁴³ mention analogous anatomic states. Bodon Dobrick and Toulouse and Marchand⁴⁴ among many others, assert that they have found a useful antiepileptic adjuvant in ovarian therapy.

My experience is that in young epileptics when it is possible to regulate the menses, important improvement results, just as improvement follows regulation of gastric or intestinal function if this has been impaired. In general among menopausal women "anti climacteric" treatment is equally beneficial.

⁴³Claude and Schmiergeld: Etude de 17 cas d'épilepsie au point de vue des glandes à sécrétion interne. *Encephale*, No. 1, 1919.

⁴⁴(a) Toulouse: Thérapeutique ovarienne chez les épileptiques *Rev. de Psychiat.*, 1899.

(b) Bodon, cit. by Marchand. Note (32c), page 231.

(c) Dobrick: *Idem id.*

CHAPTER XVII

METABOLIC DISTURBANCES

Outline

In this chapter we shall study the following:

- (a)

{	Obesity	
	Localized adiposes	{ Abdominal adiposis Adiposis and lipomatosis of the limbs
	Symmetrical lipomatosis	
	Adiposis and Dercum's painful lipomatosis	
	Barraquer's progressive lipodystrophia	
{	Climacteric thinness	{ Hyperthyroid Hypophyseal cachexia
- (b) Diabetes
- (c) { Gout
Chronic rheumatism
- (d) Late osteomalacia

Some of the above, as studied in other chapters, are direct *symptoms* of the menopausal crisis. Others are *complications* of the crisis or to put it differently, they are diseases of well-defined etiology and pathogenesis, whose appearance is favored by the critical age.

Climacteric Obesity. Errors in Statistics

Obesity, properly speaking or *generalized adiposis* is one of the consequences which the laity correctly attributes to the menopause. Indeed everyone has noted that a great number of women who have always been thin, take on weight on reaching the critical age. Elsewhere (page 35) I referred to certain writers who claim, with the pedantic security of some statisticians, that no such increase in weight occurs at the climacteric, since a number of obese women began to gain weight before the age which is considered critical—forty to fifty years. I expressed my opinion that these statistics have no value in the face of a

repeated fact which anyone can prove. It may be said that in biology statistics at times are a means of falsifying the truth through data.

The error in these statistics is rooted in three circumstances.

(1) *As I have said repeatedly the climacteric crisis begins long before the time when the menses are disturbed.* Compilers of statistics take this latter occurrence as a guide in fixing the beginning of the climacteric. But a disturbance which begins, for example, in the thirty-fifth year may be clearly climacteric, although the menstrual cessation does not occur until forty-five. This is true of certain nervous disturbances as we have seen. (2) It is probable, since no mention is made of the menstrual state, the age only being given, that *in many of the cases included in these statistics the early appearance of the obesity is due precisely to a premature ovarian insufficiency.* My experience in this connection is decisive. The greater part of the obesities of young women coincide with symptoms of insufficiency of the ovary.¹ My opinion here agrees with that of Godart,² Berkovitch³ and others. (3) *In many cases it is not a question of great obesities, such as are called to the attention of physicians, but of a discrete adiposity, characterized more by quality than by quantity.* As I have said elsewhere "women who were thin before the menopause may not grow fat. But, slowly, after the climacteric, or the preclimacteric epoch, the morphology changes. It acquires a distinct type, becoming more massive, and is definite up to old age. In women who were previously corpulent these changes also occur. They are clearly marked and there is more or less increase in weight."

Symptoms of Climacteric Obesity.—The characteristics of this *climacteric obesity* are well known. *The fat accumulates preferably in certain regions*—in the epigastrium, throughout the abdominal wall, on the thighs and gluteal region, in the submammary tissue, making the curve of the bust very prominent, on the posterior part of the neck, over the first dorsal and last

¹Marañón: Op. cit., note (19), page 124.

²Godart: Ménopause précoce et obésité. Thèse de Paris, 1908.

³Berkovitch: De l'obésité d'origine génitale chez la femme. Thèse de Paris, 1908.

cervical vertebrae exaggeratedly accentuating the curve there, under the chin which folds and at times doubles, and on the arms which acquire an exaggerated plumpness. In short *the whole body acquires a characteristic type which may exist without there being necessarily a great increase in weight.*

According to my observation, this peculiar increase of subcutaneous fat is apt to begin on the abdomen, arms and shoulders. It may even begin here several years before the appearance of the properly critical symptoms. The abdominal fat is likely to constitute one of the first esthetic worries of the feminine climacteric. But no worry attaches to the over-rounding of the arms and shoulders, for this allows the woman to display, in décolleté, a contour more statuesque, perhaps, than ever before.

Another very peculiar characteristic of climacteric adiposity is its resistance to treatment. Women who care much for their persons know that on reaching forty they must increase their efforts to combat it. They also know that it is particularly the adiposities which begin to deform the lines of the abdomen, bust and thighs which desperately resist diet, medication, and massage.

Grades of Obesity.—Naturally there are many grades of climacteric obesity. In women so predisposed, *especially those who give themselves no care, particularly if they are multiparas*, this accumulation of fat becomes really abundant, and gives the body at last a disagreeable appearance. The neck entirely loses its lines, folded in front into a full double chin and thickened behind by a true juxtaspinal adipose deposit. The thickened breasts, like enormous lipomata, sag down sometimes to the epigastric region. The abdomen wrinkles in several fatty folds which may even hang over the mons veneris. The circumference of the thighs is greatly increased. The upper arm acquires a fullness which really reminds one of the form of a ham and because of its firm consistency has given rise to the expression “hamified” [*ajamonamiento*] with which the common people refer to this transformation in women. But, in general, even in extreme cases, climacteric obesity is characterized more by the deformation of the figure than by extraordinary increase in weight. Colossal obesities are not apt to be developed after the menopause.

Pathogenesis of Climacteric Fattening. The Ovarian Factor.—

What is the pathogenesis of climacteric obesity? In this, as in any other variety of obesity we must consider the endogenous, or endocrine, factors, and the exogenous, such as the dietetic, factors. All of the endocrines which intervene in the crisis of the climacteric have a positive influence on general metabolism, and therefore, in certain fundamental conditions may cause obesity. *Ovarian insufficiency alone may produce a slowing of the general metabolism which would be propitious for the development of fat in excess.* This is proved through common observation, upon which I need not dwell, of the frequency with which adipose tissue increases in castrated women or in castrated animals. The experiments of Curatolo and Taruli, of Charrin and Jardry, of Patchner, and especially those of Loewy and Richter, have demonstrated that castration markedly slows the rhythm of metabolism by deadening oxidation and, therefore, predisposing to obesity. The objections raised against these conclusions, which are so in keeping with clinical findings, have not impeached their value.*

Intervention of the Thyroid in Obesity.—The thyroid is known to have a strong and direct influence upon general metabolism, accelerating it. Hence the thyroid has correctly been called

*For details and a bibliography on this question, see my text (cited note 19, page 124). There I fully discussed this problem. Among the opponents of this point of view Marcel Labbé merits special attention, as he is a master clinician. In several of his publications, but particularly in his recent monograph, *La obesidad y su tratamiento* (Paracelso, Madrid, 1924), he considers the fat increase due to genital deficiency as not having been well demonstrated. Indeed he cites many examples of castrated men and women, and animals, who did not put on weight and, on the contrary, he gives cases of people and beasts who did fatten although the genital apparatus was wholly sound. But it is clear that the demonstrative value of these cases is very restricted. We know that genital insufficiency is a predisposing factor in obesity, through its retarding action on metabolism. Writers mentioned earlier have demonstrated this experimentally. With Carrasco I have confirmed it in numerous cases of ovarian insufficiency in the clinic. *Op. cit.*, note (16), page 76, and *La valeur du métabolisme basal en clinique*. Réunion internationale de la Société de Biologie, Paris, June 1924. This lessening of oxidation may be balanced by a proper diet and vigorous exercise. Thanks to these the individual may avoid putting on weight, and this doubtless is, aside from other endocrine complications, what occurs in the case of the lean eunuchs, whom Labbé saw running before the royal carriages in Constantinople. In the same way there may be uncastrated individuals with a metabolism which is not retarded who nevertheless put on weight if overeating is indulged in combined with no exercise. Such is the case of the uncastrated bulls, cited by Labbé, which are fattened by Argentine cattlemen. But the almost perfect coincidence that we see in our clinics between obesity and hypogonitalism (surgical castration, juvenile genital insufficiency, climacteric, etc.), linked to the metabolic data just explained, leaves no doubt as to the predisposing influence of genital insufficiency. Aside from the quantitative factor, let me repeat, there is a qualitative, the peculiar distribution of fat which is never lacking even when there is no true obesity.

“the bellows of organic combustion.” Thus when this gland is functionally deficient, the general metabolism is retarded and obesity results. Von Noorden⁵ assumes that all adiposity of endogenous origin formerly called “constitutional obesities” are hypothyroid. I go even further in my interpretation. I believe that even exogenous obesities, those most clearly dependent upon overeating or lack of exercise, require a *predisposing* endogenous factor, a metabolism which is rather inactive because of a rather inactive endocrine system. This endogenous factor explains why one individual who eats a great deal puts on weight while another eating the same amount remains thin. Note that I say an inactive “endocrine system.” While I admit that here the thyroid is the chief element, I believe that other glands, the hypophysis and gonads, collaborate with it, just as in the regulation of carbohydrate metabolism other glands, like the thyroid and suprarenals collaborate with the pancreas, although secondarily.

Now *in my opinion menopausal obesity is precisely one of those obesities which depends least on hypothyroidism.* I have already said that a tendency to hypothyroidism is not apt to occur in many women in the change of life, at least not in the early phases which correspond exactly to the beginning of the adiposity. The general tendency is toward hyperthyroidism which we know tends to produce thinness. Clinically, climacteric obesity does not produce typical thyroid obesity. This latter is more uniform, more voluminous and is accompanied by symptomatic details lacking in the other. Moreover it yields to thyroid medication which, as we shall see, is not apt to be very effective in the treatment of menopausal fattening. We shall, then, admit the existence of a hypothyroid factor in the genesis of this symptom only in certain cases wherein there are clear symptoms of hypothyroidism from the beginning of the crisis and also in the last phases of the climacteric in which a functional diminution of the thyroid very often does occur. This latter may be seen even in those cases which were originally hyperthyroid.

⁵Von Noorden: Op. cit., note (33), page 35.

Rôle of Hypopituitarism in the Genesis of Menopausal Obesity

*In my opinion the hypophysis is important in the pathogenesis of climacteric obesity,*⁶ probably collaborating with the genital insufficiency and the exogenous factors which we shall study later. In making this statement I rely on the fact of *the absolute clinical identity between the morphology of climacteric obesity, and naturally the obesity of castrated women, and that of obesity hypophyseal in origin.* In cases with a primary hypophyseal lesion the syndrome resulting from the functional insufficiency is manifested among other symptoms by an adiposity, usually not very important in amount, but very characteristically deposited on the abdomen, hips, thighs, bust and neck; that is to say, in the same sites elected in hypogenital insufficiency. This alone makes it very difficult to differentiate between a castrate and a hypopituitary condition (Biedl⁷). On the other hand, I have already explained that everything appears to indicate that hypophyseal insufficiency is not an infrequent element in the climacteric crisis.

I particularly stress the development of *abdominal obesity*. In previous publications I have expressed my belief that in this "qualitative adiposity" (rather than the "quantitative") which is originated by hypophyseal insufficiency the most typical localization is the increase of the panniculus adiposus in the anterior

⁶Perhaps this phrase of mine was the one which caused Marcel Labbé (in the book mentioned in note 4, page 239) to make the following statement which I must explain. He says, "Little by little there has been imposed upon physicians the idea of an obesity related to insufficiencies of the hypophysis. And certain writers, like Marañón have come to think hypophyseal disturbance is the foundation of all obesities, as thyroid insufficiency is the foundation of myxedema." The difference between my statement, which refers solely to climacteric obesity, and my learned friend's comment is evident. He attributes to me a belief in a hypophyseal pathogenesis in "all obesities." Not only have I never thought so, but I have always insisted on considering as abusive the excessive generalization of the "hypophyseal obesity" concept in several of my articles (some published in French like that cited in note 25, page 112. Especially in my volume: "*Problemas actuales de la doctrina de las secreciones internas*", have I summed up my ideas on the principal endocrine problems. In this book I explicitly stated (page 222) "We should be prudent, however, not to give an excessive latitude to the concept of hypophyseal obesity. Hypophyseal obesities have their characters of well-defined topographic distribution. And we are permitted to make this diagnosis only in cases wherein these characters exist with complete clarity, and especially when they are accompanied by some focal symptoms of a pituitary tumor or other manifestations of hypophyseal origin such as diabetes insipidus. Hence we should refrain from considering as of hypophyseal origin many types of obesity which have until now been lightly so included,—such as the postinfectious obesities (Massalongo), and the frequent prepubertal obesities." I believe that on this point⁷ my restrictions are even more exacting than those of M. Labbé.

⁷Biedl: Op. cit., note (15), page 19.

abdominal wall.⁸ In assuming this hypopituitary intervention I rely upon the fact that in cases with a primary hypophyseal lesion the first adipose phenomenon, at times the only one, is precisely this abdominal fattening. In the last few months I have observed a case of enormous ventral adiposity caused by a hypophyseal hemorrhage. This condition was verified at autopsy, there being no other neighboring lesion, a finding which, I believe, proves my hypothesis irrefutably.⁹ Now, in the climacteric the predominant element is this same abdominal adiposity. It is the earliest sign, the "curve of prosperity" which warns of old age and at times the most salient, even giving rise to the syndrome of false pregnancy which we shall study presently. We may say, perhaps too arbitrarily, that in climacteric obesity abdominal adiposity corresponds to hypopituitarism and that of the hips, gluteal region and retromammary tissue to gonadal insufficiency.¹⁰

Exogenous Factors in the Obesity of Menopausal Women.—

In the production of climacteric obesity as in all obesity exogenous factors collaborate with the endogenous. These exogenous factors are overeating and too little exercise. In Spain, especially in the southern part, a great many women shut themselves up in the house at the passing of first youth, when they begin to have children or even if they have none. But for the daily visit to the nearest church their lives are no different from the hygienic point of view, than the purely vegetative life of the inmates of the harem. Women who come from villages and small towns to my clinic repeatedly tell me the same thing—"I almost never go out of the house; only to go to mass or to the novena." As for nutrition, while in general starches and fats are apt to predominate in the greater part of Spanish cooking, the amount is not likely to be excessive in most cases. *But we must take into account the fact that overnutrition is relative. Each organism has its saturation point, hence an apparently moderate ration may be*

⁸Marañón: Op. cit., note (5), page 68.

⁹I shall publish this case shortly. It is really important in the study of hypophyseal pathology.

¹⁰In this respect see Viard's thesis: *Recherches sur les rapports des trophodemes et des adiposes localisées chez la femme* (Thèse de Paris, 1913), which along with some indefensible points of view, contains others which are really sound.

excessive for a particular one. Thus some menopausal women have an endocrine system orienting them toward obesity, *predominance of hypogenitalism and perhaps hypopituitarism with the thyroid function normal or below.* They become obstinately fat although they undergo unheard of deprivations in diet. On the contrary, other menopausal women whose endocrine system is oriented toward thinness, *a predominance of hyperthyroidism,* cannot put on weight even through excessive eating. Thus we may say further that in some cases the crisis of sexual subsidence coincides with an extraordinary increase in appetite.

Localized Adiposities

I referred above to *local adiposities*, that is, to the *preponderant accumulation of fat in special regions of the body.* Such deposits are not rare in the critical age. As I have already indicated, they depend on various endocrine disturbances, probably in collaboration with the vegetative nervous system as Pende assumes,¹¹ establishing an indubitable pathogenetic relation between the localized adiposities and the *trophedema* described by Meige. Let us study *abdominal adiposities and those of the limbs.*

Abdominal Adiposis. Its Relation to False Pregnancy. Psychic-Somatic Complex in This Syndrome.—*In the menopause the most frequent form of adiposity is that localized on the abdomen, which may become extraordinarily large and simulate the gravid state.* The majority of the cases of "false pregnancy," described in the literature, were, in my opinion, cases of this kind. Consequently we shall consider this curious affection here and not in the chapter on nervous disturbances, as is usually done. Of course the subjective conviction of pregnancy when none exists always presupposes an abnormal mental state. But aside from this the actual fact of ventral deformity may be of grave significance. (Fig. 11.)

In women whose desire to remain young makes them forget how old they are and especially in those who are prematurely menopausal, it is really striking to note how the suppression, often abrupt, of the menses coincides *with a gradual increase in the*

¹¹Pende: Sistema nervioso simpatico e glandula á secreción interna. Distrofie endocrino-simpatiche. Il Tommasi, 1909.

size of the abdomen. The woman's conviction of her condition, which may lead to a medical diagnosis of pregnancy, depends upon her psychic state. There is usually an hysteric temperament in these cases which is not only favorable to the rise of the



Fig. 11.—Abdominal adiposis in a case of hypopituitary-genital insufficiency, with premature menopause and false pregnancy. (Personal case.)

false hopes through signs which have a certain value, *but these women are apt to be disposed to this special chimera of pregnancy. This inclination may be due to an unfulfilled desire to have chil-*

dren, or to an effort at self-deception that they have not yet lost sexual power. Here are examples of both "psychologic types" of women with false pregnancy.

CASE 56.—A. de S. A woman of forty; always obese, with scanty menses; sterile. Hence she had a certain ovarian or hypophyseal insufficiency. She had lived several years with her lover in the vain hope of his marrying her. She believed that if she could have a child he would do so *and she lived on tormented by this longing for offspring.* She had vainly consulted many specialists and had taken innumerable remedies without result. At forty the irregular menses were suddenly suppressed and the abdomen increased rapidly in size, resembling with considerable exactness the gravid one. When the menses failed to appear in the second month she was convinced of being pregnant. I saw her in the fifth month. Objective examination revealed an enormous panniculus and a nongravid uterus. The endocrine and psychic antecedents enabled me to rectify her mistake as to her condition. Hypophyseal, ovarian and thyroid therapy reduced the enlargement, thus confirming my diagnosis.

CASE 57.—M. L. B. English. Forty-six years old; thin; without endocrine antecedents; married, with two children, the last born eight years ago; very passionate but without psychic abnormalities; intelligent; very careful of her beauty which scarcely had begun to fade. This was probably due to the fact that the menses were still regular. A certain tendency to put on weight which was corrected by diet and exercise gave warning of the approaching climacteric. She suffered from a profound depression because her lover of several years had grown cold. *She attributed this to the fact that she was beginning to lose her physical attractiveness and to look old* in spite of her efforts. I happened to know that this indifference was due to a premature sexual decline on his part. Her depression lasted several months, during which poor emotional control, the psychologic characteristic of the climacteric, was observed. The menses suddenly ceased and at once the abdomen increased considerably in size. Aside from the endocrine factors, her ceasing to diet and exercise probably had an influence. Suffocations now appeared

with dizziness, nausea and other symptoms which led her to believe herself pregnant. This conviction filled her with joy for it proved to her that she was not yet old. The false pregnancy lasted two months, being ended by a series of hemorrhages, very close together, and a lessening of the ventral adiposity through hypophyseal-thyro-ovarian therapy.

There are cases wherein the *psychosomatic complex of false pregnancy* is produced in all good faith in women who have no psychologic bias. This happens, for example, in some multiparas who have had children up to the very border of the menopause. They have been accustomed to giving a gravid interpretation to this increase in the size of the abdomen. I have seen various cases of this kind. Here is one which I have already published.

CASE 48.—S. de C. An Andalusian of forty-five; always healthy; 10 children, born at intervals of two to three years, the last three years ago. Menses very regular between pregnancies. Suddenly they stopped and shortly thereafter abdominal enlargement began. *As usual she considered herself pregnant.* The increase in the abdomen was considerable in the following months and was complicated with swelling of the legs and later great nervousness, oppressions, etc. The physicians who attended her thought this was a complication of pregnancy or, more likely, symptoms of ascites. My diagnosis of hypophyseal-genital adiposity was confirmed by the success of the corresponding opotherapeutic remedies. These caused the fat on the abdomen to disappear rapidly and also caused the reappearance of the menses.

According to Kisch¹² the serous fluid which at times flows from the nipples (see page 177) contributes to the autosuggestion of pregnancy, and the intestinal movements, so frequent in this age, are interpreted, by a nervous system prepared for such error, as fetal movements. Naturally this is especially true in nulliparas who have had no personal experience with this characteristic sensation.

There are cases wherein the fiction of pregnancy was believed by the patient, by those about her and even by her physician

¹²Kisch: Op. cit., note (13), page 19.

until the nine months had run their course—when the true condition was disclosed.¹³

Adiposis and Lipomatosis of the Limbs.—Cases of *adiposis localized on the legs* are not rare either. Sometimes this occurs in



Fig. 12.—Lipomatosis localized on the legs in a climacteric woman. (Personal case.)

¹³I may not speak here of some recent cases I have seen which were truly interesting. They demonstrated to what unbelievable lengths these women may carry their false impression. But even though the reports were disguised and given in strictly scientific form, still I should be running the risk of betraying professional confidence. Dr. Torre Blanco (*Nuevas casos de falso embarazo*, *Anales de la Academia Médico-Quirúrgica de Madrid*, 1922) has lately published several curious cases of this very syndrome.

a diffuse form, again in a lipomatous form. Various cases have been reported. I have seen some such in obese women as well as in those who, if not thin, were at least only moderately fat. *But the condition was almost always in relation to the climacteric crisis.* Fig. 12 shows a typical case of this lipomatosis whose rebelliousness to treatment is very marked.

Such adiposes and lipomatoses are very common on the arms. These, like those of the legs may be accompanied by discomfort or frank pain, as in *Dercum's disease*.

Symmetrical Lipomatosis

Intimately related to these phenomena is the so-called *symmetrical lipomatosis*. In reality it is distinguished from them only by the perfect symmetry of the lipomas and by their clear delimitation from the neighboring fat. In short they give a "tumoral" impression which ordinary adiposes and lipomatoses do not, appearing more like mere accumulations of general fat. The so-called *supraclavicular lipomas* and *pseudolipomas* appear frequently in the *climacteric* or *preclimacteric* stage. Sometimes these fatty deposits deform the shoulder line very early. They have been related to different endocrine disturbances, to the thyroid by Levi and Rothschild¹⁴ and to the hypophysis by Marimón.¹⁵ But in my judgment it is climacteric ovarian insufficiency with its train of neuroendocrine reactions which is most intimately connected with these phenomena. Sometimes the symmetrical lipomatoses are painful and then I regard them as an indication of Dercum's syndrome, which we must consider here.

Dercum's Syndrome and the Menopause. Endocrine Factor and Nervous Factor

The symptoms of this syndrome are well known. They are limited to adiposity, painful on pressure and, less often, spontaneously. The adiposity may affect three types: (1) *Generalized diffuse*, that is, extended over all the subcutaneous tissue. (2) *Localized diffuse*, when it is limited to certain regions as the arms,

¹⁴Levi et Rothschild: Op. cit., note (1), page 38.

¹⁵Marimón: Lipomatosis simétrica. Revista de Ciencias Médicas de Barcelona, 1913.

legs, etc. (3) *Nodular*, which is like a common lipomatosis irregular or symmetrical, painful on pressure.

It is a common observation that these *painful adiposities* are more frequent after the menopause, or after castration according to Sicard and Roussy, and Sicard and Berkovitch.¹⁶ They improve under ovarian treatment. Hence these writers reach the conclusion that *Dercum's disease is due principally to an ovarian insufficiency.*

This hypothesis does not exclude the fact that *probably the hypophysis and thyroid also intervene*, as several writers have supposed, *besides a nervous factor, trophic and psychic.*

Here I refer, on one side, to a trophic influence, exercised by the vegetative system like that admitted as intervening in the other affections of the "endocrino-sympathetic" group; and on the other side, to the possibility that perhaps the nervous temperament of the patient may also enter into the production of the "pain" symptom. In regarding this last as possible we return somewhat to Kaplan and Fedoroff's old point of view. In the first edition of my book *Las glandulas de secreción interna y las enfermedades de la nutrición*, I denied absolutely this hysteric pathogenesis of Dercum's disease. But later careful observation of many cases has convinced me that it is not clearly a hysteric manifestation, as Kaplan and Fedoroff believed, *but rather that the difference between ordinary nonpainful adiposes and lipomatoses and Dercum's disease (which is exactly like them in morphology and its mode of presentation) consists, perhaps, only in the patient's exaggerated susceptibility to pain. Sometimes this last is a true hysteria, sometimes a simple neurosis.*¹⁷ The fact is that there is an insensible gradation between those adipose women who do not complain that their fat oppresses them, those who complain only a little, and those who complain a great deal. Those who do not are apt to be calm and apathetic. Those who do are very nervous, presenting every gradation from a somewhat excitable temperament up to hysteria. For the rest, the disease in almost all cases coincides with the critical age.

¹⁶See a résumé of the question and the bibliography in my book, cited, note (19), page 124, and in that of Castellino y Pende, note (1), page 73.

¹⁷Op. cit., note (4), page 239. M. Labbé expressed himself in this way. He stated that alcoholics are not rare among the obese who frequently present various types of pain, "without justifying the description of a special form of obesity, like that which Dercum has tried to define." For H. Zondek—*Die Erkrankungen der Endokrinen Drüsen*, Berlin, 1923—, the sensibility is plainly due to the dilatation of the tissues through the accumulation of fat.

Progressive Lipodystrophia. Barraquer's Disease.

In this connection I should mention the curious syndrome described by my compatriot Barraquer under the name *progressive lipodystrophia* and already known to the scientific world as *Bar-*



Fig. 13.—Progressive lipodystrophia beginning in the climacteric, combined with premature senility and hyperthyroidism. (Marañón and Pardo.)

raquer's or *Barraquer-Simon's disease*.¹⁸ I feel honored that I

¹⁸See the bibliographia on the question in:

(a) Barraquer: *La lipodistrofia progresiva*. Archivos de Endocrinología y Nutrición, Madrid, June, 1924.

(b) Marañón: Un caso de lipodistrofia progresiva con curiosas alteraciones endocrinas. Archivos de Neurología, Madrid, 1920, No. 3.

(c) Marañón y Pardo: Un nuevo caso de enfermedad de Barraquer. R. A. de Medicina de Madrid, 1924.

(d) Boissonnas: Sur la lipodistrophie progressive, Rev. Neuro, 1919.

assisted in having the term accepted. This syndrome consists of an atrophy of the subcutaneous adipose tissue in the upper half of the body while this tissue remains normal, or only slightly increased perhaps, in the lower half. Inspection of Fig. 13 serves better than any description. I especially stressed the precocity and intensity of Bichatt's fatty bolus while giving to the face an expression of extreme thinness, "like a skull," which is clearly seen in this figure and which is not common in other emaciations unless they are in their extreme stages. Cases seen in these later years have established a relation between this form of lipomatosis and certain endocrine disturbances. The patient shown in Fig. 13 and others which I have seen lately *make me think that one of the endocrine states perhaps most frequently associated with this syndrome is the hyperthyroidism of the climacteric.*

I mention hyperthyroidism here not only for this apparent relationship but also because of its appearance in cases of lipomatosis and adiposis of the lower limbs, previously described, and in cases with trophedema of the lower limbs which I shall soon consider. Nevertheless the distinction is clear. In progressive dystrophia there is a thinning in the upper half of the body and *fusion with Bichat's bolus*; this, and not the adiposis or pseudoadiposis of the lower limbs is the characteristic mark of the process.

Pathogenesis of All These Processes. Their Relation to Quincke's Disease and Meige's Trophedema

All these processes which we have studied, localized adiposis, lipomatosis, symmetrical lipomatosis, Dercum's disease, and Barraquer's disease, appear to depend on a metabolic defect which is linked with thyroid, hypophyseal and genital disturbances. Again I tirelessly repeat that we do not understand the intimate mechanism of this relation. *My statement which does not assume to pass as an hypothesis is based on clinical conjecture which is, nevertheless, important.* To this assumed endocrine factor *there should be added a vegetative nervous factor*, for which reason, as I said before, Pende includes all these states under *endocrino-sympathetic dystrophies*. It would be more exact to say *endocrino-*

vegetative. This vegetative nervous factor explains the localization as regards symmetry, segmentary distribution, etc., of the lesions which cannot be explained by the humoral element alone. In Dercum's disease a *central nervous element also enters*.

Let me note in closing that several of these processes of localized adiposis and lipomatosis are related to two other states. These are *Quincke's fugitive circumscribed edema* and *Meige's trophoedema*. I shall speak of the first in Chapter XXII. Clinically it is well differentiated from the lipomatoses and adiposes by its short duration and by its elastic consistency which is clearly distinguished from mere accumulations of fat.

As for trophedema, its clinical delimitation from some of the localized adiposes in the arms or legs is very indistinct. Bauer and Desbouis, for example, have described¹⁹ a case of "*trophoedema*" of the arms initiated in the menopause, which was difficult to differentiate from the simple adiposis mentioned above. An endocrino-vegetative pathogenesis is also involved in trophedema and is, therefore, common in all such conditions. Nevertheless, the cases which I have seen of Meige's disease permit me to assume that this distinction is possible in the majority of cases, if we rely on the uniform edema which is distinct from the uneven and less elastic consistency of the adiposis, and on the younger age in which it commonly appears.²⁰

Climacteric Loss of Weight

The majority of menopausal women put on weight as I have said. While rarely some maintain an unvarying weight, others, a considerable number, lose weight. According to Tilt,²¹ of 282 women observed five years after definite cessation of the periods, 121 had fattened, 71 had not varied in weight and 90 had grown thin. These data coincide approximately with those of my experience, except that I believe there are not as many women as Tilt indicates whose weight does not vary in the critical age.

Hyperthyroid Pathogenesis of Loss of Weight.—One finds

¹⁹Bauer and Desbouis: Trophedeme des membres supérieurs ayant éclaté a la ménopause. Nouv. Iconographie de la Salpêtrière, 1910.

²⁰(a) See an excellent study of trophedema in Rietti's article Sul trofoedema cronica di Meige. Policlinico, Sez. Med., 1924; this contains careful diagnostic consideration of all these similar states. Also (b) Pereira's article Un caso de trofoedema. Siglo Médico, July, 1923.

²¹Tilt: Op. cit., note (10), page 102.

scarcely any data on this *menopausal loss of weight* which, as I said, is frequent. The woman may lose weight during the crisis because of its coincidence with various wasting processes such as digestive diseases, diabetes or cancer. I do not refer to these cases wherein clinical observation quickly discovers the cause of the loss of weight. I refer to those cases wherein a careful examination excludes the existence of wasting diseases. The loss of weight is then generally attributed through an arbitrary diagnosis to some such case as anemia or neurasthenia. But I believe that the responsibility *lies in true attacks of hyperthyroidism*, whose frequency in this age I have mentioned so often. (Chapters III and XVIII.)

This loss of weight is characterized and diagnosed by the absence of wasting diseases; by the healthy appearance which the woman retains, indicating "physiologic loss of weight"; by its spontaneous variations and because it is accompanied by other hyperthyroid symptoms, such as tremor, vasomotor irritability, tachycardia and perhaps hypertrophy of the thyroid. I shall consider this condition at greater length in the next chapter.

Diagnostic Errors.—From the clinical point of view it appears to me as very important to recognize that this loss of weight occurring before or during the menopausal crisis is plainly of endocrine origin (hyperthyroid) and when misinterpreted gives rise to grave errors in diagnosis, several instances of which I have seen. Together with the occurrences of hemorrhage, the condition may be thought a cancerous process of the uterus, as happened in the following example:

CASE 59.—C. R. Woman of forty-nine. In late years she had put on weight without being obese. Menstrual irregularity with hemorrhages began at the forty-sixth year and a state of very marked emotional erethism. Her husband suffered several important reverses which worried her greatly, *hence there was a clear emotional etiology for her condition.* At this stage the hemorrhages became very profuse and she began to lose weight rapidly. Moreover she was very asthenic; no appetite. All this and the fact that her mother had died of uterine cancer brought a diagnosis of probable malignancy. She was referred to a gynecologist who could not find the assumed lesion and it was then

that I saw her. I found a permanent tachycardia of 115, fine tremor, and intense vasomotor irritability. This permitted me to change the gloomy prognosis to the benign one of menopausal hyperthyroidism. The later course of the condition confirmed this diagnosis fully. Six years later complete amenorrhea. She has put on weight and is perfectly well.

In the next chapter I shall refer to other sources of error in diagnosing cases of climacteric hyperthyroidism as cancer of the stomach or less serious processes such as anemia, chlorosis, neurasthenia, or phosphaturia.

Hypophyseal Cachexia.—Another form which is less frequent and occurs later than that which we have just studied is loss of weight of *hypophyseal origin*. I have already spoken (pages 67 and 105) of the probable hypophyseal origin of the cachectic thinness of those women who have exhausted a previously precarious physical energy in a very active genital life, frequent pregnancies, parturitions and lactations. In such women the menopause, making the hypofunction of the pituitary more marked, also accentuates this loss of weight. I shall return to this question in the next chapter.

Diabetes and Menopause. Chronologic Data

The relation of diabetes to the *menopause* is very interesting. Tilt²³ states that menopausal women frequently become diabetic and the same statement has been made by Bouchardt,²⁴ Lecorché,²⁵ Leclercq²⁶ and others. Of recent works on diabetes, Noorden²⁷ gives the age of fifty as the one showing a large percentage of the most advanced diabetes. Lepine²⁸ from his own statistics and from a comparison of various writers deduces that the years from forty to sixty are the most propitious for the appearance of this disease. MacClean²⁹ observes that the curve of alimentary hyperglycemia is developed in the mature man and in the old according to a "diabetic type," although there is no glycosuria, which indicates an evident predisposition to diabetes. But none

²³Tilt: Op. cit., note (10), page 102.

²⁴Bouchardt: Monographie sur la diabète, Paris, 1875.

²⁵Lecorché: Traité du diabète, Paris, 1877.

²⁶Leclercq: Les maladies de la cinquantaine, Paris, 1922.

²⁷Noorden: Die Zuckerkrankheiten, Berlin, 1922, ed. 6.

²⁸Lepine: Le diabète sucré, Paris, 1909.

²⁹MacClean: Insulin, Lancet, 1923, p. 1041.

of these writers relate this circumstance to the menopause. On the contrary, Dalché expressly fixes this relationship and attributes to ovarian insufficiency an undoubted rôle in the pathogenesis of certain cases of diabetes,³⁰ Aschner³¹ makes the same statement "the critical time *par excellence* for diabetes is the climacteric, whether the pancreas takes part in it or not."

I have studied every detail of this question,³² and have *established the fact, undoubted in my opinion, that ovarian insufficiency—in general genital insufficiency—is a very important predisposing factor in certain diabetic states*. In the first place I base this on the well-known coincidence of diabetes with the age of sexual subsidence, which according to my data, in agreement with that of the writers mentioned, is an almost constant finding. *Of 345 diabetic patients whom I have studied in the last few years, the first symptoms appeared between the fortieth and fiftieth year in 72 per cent.* Many women spontaneously refer the beginning of their symptoms to the epoch of menstrual cessation. In other cases the diabetes comes on, one, two or three years after the cessation of the menses. But this difference is explained when we remember that almost always we consider as the "beginning" of the diabetes its "discovery" by the patient himself. This generally occurs some time after the real beginning of the disease which is apt to be very insidious.

Experimentation reinforces this clinical argument since alimentary glycosuria according to Stolper³³ and adrenalin glycosuria according to Cristofolletti³⁴ are produced with greater facility in castrated animals than in the uncastrated. Adler³⁵ and Baillod³⁶ have made the same observation in the castrated woman. I have confirmed these results as to glycosuria and glycemia in castrated animals.³⁷

³⁰Dalché: Opothérapie, puberté, glandes endocrines, Paris, 1915.

³¹Aschner: Beziehungen der Drüsen mit innerer Sekretion zum weiblichen Genitale. In *Biologie und Pathologie des Weibes*, Berlin, 1924, i.

³²Marañón: Op. cit., note (19), page 124.

³³Stolper: Ovarium und Stoffwechsel, Gynäk, Rundschau, 1913, vi.

³⁴Cristofolletti: Op. cit., note (26), page 62.

³⁵Adler: Op. cit., note (28), page 62.

³⁶Baillod: De l'influence de l'ovaire sur les variations de la glycémie après l'injection d'adrenaline. *Korrespondenz f. Schw. Aerzt.* 1919, No. 50.

³⁷(a) Marañón: Op. cit., note (27), page 62. (b) Marañón y Rosique: Glucemia e hipertiroidismo. *Bol. de la Soc. Esp. de Biol.*, 1916.

Moreover, I cite the studies of Parisot³⁸ who found evident lesions of the ovary and of the masculine interstitial gland in diabetic subjects and animals made glycosuric.

Mechanism of Climacteric Predisposition to Diabetes.—Note that I have spoken of genital insufficiency only as a *predisposing factor in glycosuria*. Its action is probably limited to provoking in the organism a special neuro-endocrine modification which facilitates the activation of the directly glycosuric factors. The proof of this is that glycosuria does not appear spontaneously after castration. Even the hyperglycemia itself does not come on, as Rosique and I have demonstrated, until after a certain period of latency.

What is this predisposing mechanism that develops after the loss of ovarian function? I cannot attempt to give it in detail without running into an overbold hypothesis, which we should carefully avoid in this study. But the probability is that the two glandular reactions most frequently accompanying genital insufficiency in the climacteric crisis, the suprarenal and thyroid hyperfunction, are precisely the conditions favorable to the production of glycosuria. I have spoken in Chapter IV, page 51, of the possible relation of climacteric hyperadrenalism to glycosuria. As for the relation of hyperthyroidism to glycosuric and diabetic states, this is now well established.³⁹ The slowness with which these reactions develop after castration would explain this period of latency to which I referred above.

On the other hand, it must not be forgotten that this is the age wherein *the first symptoms of sclerosis appear in the vessels of the pancreas*, as Fahar⁴⁰ has noted. Finally, as we saw in the proper chapter, individuals in this age are exposed in greater proportion than others *to the exogenous and secondary factors of diabetes*, such as over-eating, emotions and remote consequences of syphilis.

³⁸(a) Parisot: Les troubles de la fonction génitale chez les diabétiques. Leur pathogénie. Bull. de la Soc. Méd. des Hôpitaux de Paris, 1911. (b) Parisot: Lésions des glands génitales chez les diabétiques et chez les animaux rendus expérimentalement glycosuriques. C. R. de la Soc. de Biol., 1911, lxxi. The counterproof of these experiments is found in Rebaudi's work. Having cauterized the corpus luteum in animals, he says he has found that a hyperplasia is produced in the endocrine islets of the pancreas. (c) Rebaudi: Eierstock, Corpus luteum und Langerhanssche Inseln, Zentralbl. f. Gynäk., 1908. It is clear that these experiments are open to severe criticism.

³⁹See the bibliographic resumé and critical comment in my book, cited in note (19), page 124, and in the interesting monograph by Bertolotti: Tiroidi e diabete mellito. Treviso, 1915.

⁴⁰Fahar: Berl. klin. Wchnschr., 1921, lvi.

Symptomatology of Climacteric Diabetes. The Prediabetic States.—Clinically this "*climacteric diabetes*" presents few peculiarities. I have already said that it generally begins in the midst of the menopause or in the perimenopausal years.

In its etiology the emotional states appear with much more frequency and intensity than in other forms of diabetes, as I have shown in a large number of my patients.

Climacteric diabetes once established, *its course is likely to be slow and mild*, according to Kisch⁴¹ and Aschner.⁴² Nevertheless, my experience of the last few years permits me to feel certain that the diabetes appearing in this age often runs a grave course. When mild it is without differentiation from the very slow diabetes of arthritis. In short, only by the time of its appearance and by no other characteristic, can a special group be made of these cases. My expression "*climacteric diabetes*" has no other meaning.

The most interesting clinical fact in these cases is their coincidence with hypertension. As I have shown⁴³ diabetes in this age is almost always linked to more or less marked arterial hypertension. In many cases I have noted that hypertension, accompanied by hyperglycemia and at times by alimentary glycosuria, precedes diabetes. For this reason I have described this syndrome as a "*prediabetic state*" which, as I said on page 180, is actually accompanied by diabetic symptoms properly speaking, such as neuralgias, loss of weight, furunculosis and pruritus. This "*prediabetic state*," a term which Kylin,⁴⁴ and Koopman,⁴⁵ and others accept, and of whose reality I am firmly convinced, appears principally in premenopausal and menopausal women, especially in those of corpulent type and with a tendency toward obesity. Here are two typical examples.

CASE 60.—S. A. Fifty years old. Multipara. Metritis at forty-six and in the course of its treatment, *sudden menopause*. In the following months *as many as 49 furuncles appeared, very rebellious*, for which she consulted me. *Urine normal whether fasting*

⁴¹Kisch: Op. cit., note (13), page 19.

⁴²Aschner: Op. cit., note (31), page 225.

⁴³Marañón: Op. cit., note (30), page 148.

⁴⁴Kylin: Op. cit., note (20), page 141.

⁴⁵Koopman: Blood Pressure and Sugar Metabolism, Endocrinology, May, 1924.

or not. *Tension* 180-110. *Glycemia* 0.21 fasting. *Alimentary glycosuria* (100 g. glucose) positive. Antidiabetic diet. Recovery.

CASE 61.—S. B. Forty-nine years old. Multipara. Very regular. At forty-six a strong emotion due to her absent husband's grave illness: thereupon *sudden menopause*. In the following days 20 g. per 1000 of sugar in the urine was found only once. *She did not again present glycosuria: but she lost weight: pruritus and great nervousness. Tension* 17.10 fasting. *Alimentary glycosuria* (100 g.) positive. *Glycemia* (fasting) 0.19 per cent. Antidiabetic diet: great improvement.

Again the diabetes of climacteric women is accompanied by more or less masked hyperthyroid symptoms which are so frequent in this age—tachycardia, fine tremor and so forth.

Gout and the Critical Age

Gout presents an undoubted chronologic relation to the menopause. That is all that can be said concretely on the subject, since there is no clinical or experimental data which demonstrates a close influence of the genital function on the metabolic disturbances which constitute gout.

The available statistics teach that in gout, women, as compared to men, give a small contingent of cases before the fortieth year. At the end of that time the figures change suddenly, and gout becomes the more frequent in women, exceeding the number of men four times. (Ceist, quoted by Kisch⁴⁶). Tilt⁴⁷ gives the following statistics:

From 20 to 30 years	56	women	died	of	gout
From 30 to 40	121	“	“	“	“
From 40 to 50	291	“	“	“	“
From 50 to 60	152	“	“	“	“
From 60 to 70	104	“	“	“	“

In Spain, where gout is much less frequent than in Saxon countries, we cannot offer as large a series as the above. But *my general impression agrees in assigning to the critical age the majority of the cases of gout which I have seen.*

⁴⁶Kisch: Op. cit., note (13), page 19.

⁴⁷Tilt: Op. cit., note (10), page 102.

Clinically, gout in this age does not differ from the ordinary forms of the disease. According to Kisch, it affects obese women principally, those with a pale, fine skin, weak muscular system, varicosities, flatulence and constipation.

Pineles⁴⁸ under the name of *pseudogout* has described an affection which is frequently presented in the critical age. It is characterized by "gouty or rheumatic pains" in the limbs, in the nape of the neck and in the shoulder. According to this writer it is related to genital insufficiency. I have already made mention of these painful states in speaking of climacteric neuralgias.

Endocrine Pathogenesis of Gout.—I can say nothing as to the pathogenic mechanism which links gout to the climacteric. Enough has been written on the possible intervention of some endocrine factors, especially thyroid insufficiency. It might be thought that these humoral factors appear in the critical age. Various writers, Lancereaux and Paulesco, Viola, Gigon and I, have noted the good effect of thyroid opotherapy in gout.⁴⁹ But the data is very uncertain and hypothetical. Recently Phronimos⁵⁰ has stressed all these points, but with some confusion, in a thesis inspired by Sainton, wherein he prolixly studies a *single case* of thyroid and testicular insufficiency accompanied by gout which improved under corresponding opotherapy.

Chronic Rheumatism and the Climacteric

The relation of the critical age to chronic rheumatism is also undoubted and also obscure. Raymond and Courtellemont,⁵¹ Renon and Hertz,⁵² Parhon and Papinian,⁵³ and many others have observed that this affection is, *in the first place, much more frequent in women than in men. In the former it elects the critical age most frequently for its appearance.* This would seem to indicate that insufficiency of the ovary at least predisposes to rheumatic attacks. This is confirmed by the fact that their onset is

⁴⁸Pineles: Op. cit., note (8), page 178.

⁴⁹See the bibliography in my book mentioned in note (19), page 124. In the last few years I have had a wider experience with the good effects of thyroid therapy in small doses as a treatment for gout in the intervals between attacks.

⁵⁰Phronimos: Goutte et syndrome d'insuffisance thyro-testiculaire, Thèse de Paris, 1918.

⁵¹Raymond and Courtellemont: Rev. Neurol, 1904.

⁵²Renon and Hertz: Rev. Neurol., 1899.

⁵³Parhon and Papinian: Press. Méd., 1905.

also favored by periods of amenorrhea, in the earlier years of life, from close-following pregnancies and very prolonged lactations⁵⁴ which exhaust the ovarian function.

Cases of spontaneous recovery during pregnancy from rheumatism of the deforming type testify to the same fact it seems to me. Levi and Rothschild⁵⁵ have described such cases, and I have published some unquestionable ones. Rather than attribute these cures to the "thyroid therapy of pregnancy," it is more logical to relate them to *the ovarian hyperactivity existing during the first months of pregnancy.* This corrects the ovarian insufficiency which collaborated in greater or less degree in the production of the rheumatism.

These facts *do not authorize us, then, to speak of an ovarian rheumatism, as some writers have done. But we may say that ovarian insufficiency predisposes to chronic rheumatism.* According to Freund⁵⁶ the forms of it which appear most frequently in the climacteric are the *exudative chronic polyarthritides* and *Heberden's nodules.* Wick⁵⁷ also insists on the frequency of the nodules in the critical period.

We do not know just how ovarian insufficiency influences the appearance of chronic rheumatism, as thyroid insufficiency does in certain cases. Probably it is an influence of very secondary rank. At present pathologists tend to attribute to infection, which is more or less latent, the majority of cases of chronic rheumatism. Certain humoral states operate in a predisposing way, causing the germs to become fixed in the articulations, thus developing the different varieties of rheumatic lesions. Among these "humoral states," which are principally gout and analogous conditions, the endocrine factors must be included, although more indirectly.⁵⁸ Let us recall that the studies of Levi and Rothschild,⁵⁹ Pende,⁶⁰

⁵⁴Todt, cit., por Parhon et Goldstein: Op. cit., note (4), page 40.

⁵⁵Levi et Rothschild: Etudes sur la physio-pathologie du corps thyroïde. 1st. Series, Paris, 1908.

⁵⁶Freund: Ueber arthritische Erkrankungen in Klimakterium. VII Kongr. österieich. Balneolog., 1912, München. med. Wchschr., 1912.

⁵⁷Wick: Ueber den Heberdenschen Knoten. Wien. med. Wchnschr., 1908, p. 311.

⁵⁸All these points of view were recently developed in our study; Marañón y Tapla: Sobre las artritis de origen dentario; suconcepto médico, etc., Revisto Española de Medicina y Cirugía (Barcelona) November, 1923.

⁵⁹Levi and Rothschild: Op. cit., note (1), page 38.

⁶⁰Pende: Op. cit., note (17), page 19.

Castellino,⁶¹ and others, establish a collaboration of thyroid and suprarenal upsets in the so-called arthritic diathesis. This is nevertheless an unquestionable clinical reality despite the disregard which it suffers at present in many medical schools.

From the symptomatic point of view rather than the chronologic coincidence between chronic rheumatism and the climacteric we may note an interesting observation. At the same time as, but independently of Massalongo⁶² I called attention to *the frequency with which chronic rheumatism occurs in women who present prematurely white hair*. Lately this has been found to be true almost without exception. As we shall see presently, it is just these women who are often hyperthyroid and their menopause is apt to be complicated. Needless to say this same observation is also applicable to men.

With these two facts and the coincidence of rheumatism and the menopause together with the frequency of other signs of endocrine upset, we are authorized to add to the usual therapy for rheumatism proper opotherapeutic remedies. Unfortunately, the influence which these exercise on the articular lesions is so indirect, as deduced from the given pathogenetic outline, that improvement is not always brilliant and when it does occur, it is referable almost solely to the patient's general symptoms.

Osteomalacia and Climacteric

In certain cases osteomalacia in its onset seems to bear a relation to states of ovarian insufficiency in youth or of *physiologic climacteric*. Curschman⁶³ has recently called attention to some of these. I have seen one very typical case which was doubly interesting, considering the great rarity of this disease in Spain.⁶⁴

CASE 62.—R. P. Widow. Her father at the age of fifty began to complain of severe rheumatoid pains beginning in the ankles and knees. Later his legs began to bend, curving slightly inward. This bending increased. He died at the age of seventy-five. She

⁶¹Castellino: *Organi endocrini e diatesi*. Boll. dell Cliniche, 1912, and Rif. Médica, 1912.

⁶²Massalongo: *Endocrinopatologia é patogènesi delle osteoartropatie croniche progressive*. Riforma Médica, 1914.

⁶³Curschman: *Ueber den mono und pluriglandulären Symptomenkomplex der nichtpuerperalen Osteomalacie*, Deutsch. Arch. f. klin. Med., 1919, cxxix.

⁶⁴Recognized by my senior interne Vara Lopez.

had nine brothers, one of whom died of smallpox at thirty-four; the other brothers died at ages varying from three to five years.

As a child she had had measles and smallpox; menstruation began at fifteen. She had her first child at twenty-four. Her fourth pregnancy miscarried at five months. Four more children and two abortions followed, a total of seven children and three abortions. The last child was born in her forty-third year. Five months later a five months' miscarriage occurred. Menstrual disturbances began at forty-five; menses had always been very regular. *At forty-five, following the last period she began to have slight pain in the ankles, later this advanced to the knees, the coxofemoral articulations, and later to the bones of the pelvis.* At the same time the legs began to curve inward but she was able to walk with some effort. The inward curvature has continued for four years, becoming accentuated and progressing in such a way that the legs are now entirely crossed. This is, therefore, a typical case of *climacteric osteomalacia*. The treatment given, adrenalin, ovarian extract, and chloroform has not produced any result.

These cases, which Curschman attributes to a pluriglandular upset (ovarian, thyroid, chromaffin, parathyroid), show the influence known since classic times of the genital secretion on the pathogenesis of this process. But they disregard the second part of Fehling's classic proposition; that is, that the disease is due to an ovarian hyperfunction, including the idea of treatment by extirpation of the genital organs.

CHAPTER XVIII

ENDOCRINE SYMPTOMS

Outline

We know that in every menopause there is an endocrine symptomatology which serves as a basis for various manifestations on the part of the other organs of the body. We know, too, that the most frequent form of this endocrine reaction which we may call "normal" is hyperthyroidism, probably hypersuprarenalism and perhaps hypophyseal insufficiency.¹ But at times the endocrine manifestations acquire, through their intensity, characteristics of true complications. Then they deserve separate study *although, as is understood, the distinction between the manifestations of a "normal reaction" and those of "pathologic complication" is purely arbitrary and gradual.* Hence these endocrine complications are apt to be usually a continuation of some normal manifestations, hyperthyroidism being particularly frequent. But other types of reaction are also seen, syndromes whose pathogenesis is less clear. These we shall take up successively according to this outline.

- (a) { Hyperthyroidism
Strumitis
Myxedema, thyroid insufficiency
Thyroid instability
- (b) Suprarenal syndromes
- (c) Hypophyseal syndromes
- (d) Sexual inversion (virilism)
- (e) Multiple glandular sclerosis

Climacteric Hyperthyroidism

Symptomatology.—On page 43 the etiology and the course of this form of hyperthyroidism have already been explained which,

¹Professor Escudero—Op. cit., note (10), page 73 has recognized marked examples of this clinical picture. He has kindly proposed for this combination of genital insufficiency, hyperthyroidism and hypophyseal insufficiency, the name of Marañón's syndrome. For this I now thank him most sincerely.

to repeat, I consider as extremely frequent and important. Here we are concerned only with the symptoms.²

The clinical picture of climacteric hyperthyroidism is the same as that of ordinary hyperthyroidism, but with some peculiarities which should be pointed out in order to orient the diagnostic judgment of the practitioner. The latter is apt to keep in mind and to give an excessive value to the classic symptoms of Basedow's disease, such as goiter, exophthalmos, tachycardia and tremor, without which, especially goiter, he is not likely to think of this disease. Now of these symptoms there are two, goiter and exophthalmos, which are not only not characteristic, but infrequent. *Indeed, rather frequently there is no true goiter in climacteric hyperthyroidism, not even the slight hypertrophy of the thyroid usual in young hyperthyroid cases.* No doubt the sclerosis of the thyroid tissue which has already begun in this age makes this congestive hypertrophy more difficult. Hence no change may be apparent in any posture or on deep and careful palpation. This absolute lack of change in the thyroid is easily seen in thin women the muscles of whose necks stand out. In other cases if it is found, either through palpation or simple inspection, the hypertrophy is generally slight and limited to the right or to the left lobe. Finally, I have already said (page 45) that a considerable percentage of these cases already had goiter, which frequently increases sensibly in size at this age.

Exophthalmos may also be wholly lacking. I have seen cases of climacteric hyperthyroidism with extreme exophthalmos but in the immense majority of cases this symptom does not exist. Other ocular symptoms, generally described in texts³ are likely to be

²In my mention of the scanty literature on climacteric hyperthyroidism I neglected to speak of the excellent article by Graff and S. Novak: *Basedow und Genitale*, Arch. f. Gynäk., 1924, cii.

³The principal ones are: *Moebius' sign*, inability to keep the eyeballs converged; *nystagmus*, generally lateral; *Stellwag's sign*, infrequency of involuntary winking; *Dalrymple's sign*, when the patient looks straight ahead, the upper lid, abnormally retracted, allows some of the supracorneal sclera to be seen; *Gräffe's sign*, failure of the upper eyelid to move downward with the eye when looking down, leaving the supracorneal sclera exposed; *Joffroy's sign*, absence of normal frontal contraction when the patient looks upward. I believe that, without inconvenience, all these useless signs may be driven from our memories if they have not gone of themselves. Their presence in a doubtful case is not sufficient to decide the diagnosis. Their absence does not invalidate a diagnosis of hyperthyroidism when other manifestations indicate it. Some signs, like *Stellwag's*, not only are infrequent, but in many cases of typical hyperthyroidism the opposite phenomenon is produced, the patient winks oftener than is normal.

lacking also with the exception of retraction of the upper lid. This retraction may be trifling perhaps but together with an increase in the brilliance of the glance gives a characteristic expression to the hyperthyroid eye, unmistakable to the practitioner. But even this may be lacking and there may be no ocular symptom whatever.

On the other hand, tachycardia is very frequent, either as an objective sign or accompanied by *paroxysmal attacks or palpitations*. This symptom is apt to be important enough to decide the diagnosis. Emotional tachycardia like that produced by the presence of the physician which neither the patient nor he consider significant, really is so. It is a lesser grade of permanent tachycardia but with the same significance.

Tremor is also observed in almost every case of climacteric hyperthyroidism, sometimes in a permanent form, again as an emotional tremor provoked by medical examination. This has a positive diagnostic value although it represents a more attenuated form of spontaneous tremor.

Loss of weight is very important and frequent. Often it is the culminating symptom of this variety of hyperthyroidism. Weight is usually lost in spurts, as may be said, and this is especially characteristic. The woman may lose several pounds in a few days, in consequence of any of the causes given above, and other hyperthyroid symptoms may coincide with this loss. Then in a few days she may wholly, or almost wholly, regain the loss. Certain women do not lose weight, the hyperthyroid syndrome coexisting with the obesity usual in this age. No doubt in these cases the thinning action of the hyperthyroid secretion is compensated by the fattening action of ovarian and perhaps hypophyseal insufficiency. The determination of the basal metabolism in many of these cases of climacteric hyperthyroidism confirms this counterposed action of the various endocrine changes which enter into the menopause and affect the nutritive index, as Carrasco and I have demonstrated. Such determinations often give moderately high results which are in great contrast to the marked intensity of the hyperthyroid syndrome.⁴

⁴Marañón and Carrasco: *Op. cit.*, note (16), page 76, and note (18), page 96.

Perhaps the most interesting of these symptoms which contribute to the climacteric hyperthyroid picture are those of the digestive apparatus. It is known that in hyperthyroidism, in



Fig. 14.—Climacteric hyperthyroidism with ocular symptoms. Great loss of weight. (Personal case.)

general, digestive disturbances are frequent, the hyperchlorhydria which I pointed out,⁵ diarrhea, well-studied by Hernando,⁶ and

⁵Marañón: Hyperclorhidrie et hypertiroidisme. *Revue de Medicine*, 1914.

⁶(a) Hernando: Algunas alteraciones gástricas de origen endocrino, *Congreso de Bilbao para el Progreso de las Ciencias*, 1919.

(b) Hernando: Algunas alteraciones intestinales de origen endocrino, *Anales de la Academia Medico-quirúrgica*, Madrid, 1919, vi.

(c) Hernando: Diarreas de origen hipertiroideo. *Anales de la Acad. Med-Quirúrg. de Madrid*, 1917-1918.

others which are less frequent. But in the last few years I have seen various cases of hyperthyroidism of acute form wherein these digestive disturbances were so marked that I felt warranted in establishing a special type of this disease which may be called "the digestive form of hyperthyroidism." Many of these cases correspond, I repeat, to climacteric hyperthyroidism.

In such cases the disease is almost always initiated suddenly by gastric or intestinal disturbance. Sometimes these are of such violence that they assume an acute gastroenteritic character with fixed course and without apparent dependence on alimentary factors. The patient, man or woman, presents a state of extremely furred tongue, lack of appetite, flatulence, various intestinal disturbances and frequently persistent biliary vomiting. In some cases this last has been diagnosed as an acute hepatic affection. These symptoms are often accompanied, especially in the first days, by a low fever.

Even when one has had experience with analogous cases it is very difficult from principle to keep one's attention upon the thyroid in the presence of this clinical picture. One thinks of everything but an attack of hyperthyroidism. We are lead to an exact diagnosis only as time passes and the gastric intolerance persists in spite of dietetic and pharmacologic treatment, and the tachycardia, tremor and disproportionate loss of weight continue and especially the state of psychic and emotional irritation.

In other patients hyperthyroidism reveals itself principally, as I have said, through diarrhea. The nervous diarrheas, rebellious to treatment, independent of food taking and directly influenced by emotional states are almost always manifestations of a more or less masked hyperthyroidism. I have often seen such cases which have unsuccessfully run the whole gamut of dietary and astringent remedies, quickly and permanently cured by anti-thyroid and ovarian treatment.

The intensity of these digestive symptoms may be such that it makes one think erroneously of grave diagnoses, including that of cancer of the digestive tract. The subjective sensation of pain in the abdominal aorta, generally erethistic in these patients, contributes to the confusion. This occurred in the following case.

CASE 63.—S. de R. Forty-three years old. Without previous disease relatable to the present state. *Rapid loss of weight, with great loss of strength, no appetite and sensation of pain on pressure in the epigastrium. Diagnosed as gastric cancer.* She was examined by Dr. Hernando who noted retraction of the upper eyelid, slight exophthalmos, severe tachycardia, exaggerated emotionalism and other symptoms which led him to diagnose the case as one of acute hyperthyroidism. I saw her later and confirmed the diagnosis. Antithyroid treatment brought quick and striking relief to the patient whose further course fully confirmed this opinion.

Here is a similar case.

CASE 64.—Doña P. T. Fifty-two years old. Multipara. Without interesting antecedents. Three years previously severe metrorrhagias appeared. Menopause followed. Two years later while the circulatory and nervous upsets still persisted, *she began to lose weight, became very pale and lost her appetite. Analysis of the gastric juice gave hypochlorhydria. Diagnosed as a probable gastric carcinoma.* Changes in the course of the disease led to a more careful examination by another consultant who found a small goiter on the left side, typical tremor, tachycardia localized erythema over the thyroid, lymphocytosis. Diagnosis, gastric form of hyperthyroidism. Six months later she recovered.

Vasomotor disturbances are most pronounced in climacteric hyperthyroidism. Generally marked in every case of Basedow's disease found in women, they are much accentuated in the menopausal form, perhaps through the assumed collaboration of hypersuprarenalism which as we know intervenes. They are presented either in the form of spontaneous sensations as *hot flushes or suffocations*, or in the form of fugitive erythematous areas appearing in different regions of the body, generally on the breast, neck and face through the influence of emotional states or light pressure. The symptom which I have described with the name of *thyroid red spot* [*mancha roja tiroidea*] is almost constant.⁷

Nervous and psychic symptoms are also very marked in climacteric hyperthyroidism. These are severe nervous irritability,

⁷See Marañón: Op. cit., note (59), page 159.

motor uneasiness, *exquisite emotionalism* and finally, psychopathies whose relation to the critical age was shown so well in a previous chapter.

Let us recall that women with climacteric hyperthyroidism sometimes present abundant and copious menses which are slow in disappearing. (Page 113.) I have also indicated the frequency with which hyperthyroid patients with severe hemorrhages and late menopause are apt to present premature whitening of the hair and at times rheumatic affections. I shall return to this point presently. Aschner⁸ has recently called attention to these hyperthyroid hemorrhages in association with "late climax." He states that in such cases the ovaries are likely to be hypertrophic and present innumerable cystic follicles which resemble in their consistency cystic goiter. In short we should think of the ovaries of myomatous women and those of women with "hemorrhagic metropathy" (page 122) as conditions varying only in degree. This condition is accentuated in case of goiter by the presence of the thyroid lesion. Hemorrhagic metropathy is of a lesser grade than the hemorrhages due to myoma.

Evolution, Prognosis and Treatment of Climacteric Hyperthyroidism.—I have already explained that the immense majority of cases of this form of hyperthyroidism *return spontaneously* to normal. Its prognosis is then, in general, benign. This circumstance, like the great rôle played by the psychic factors in its production, should be kept in mind, *in order to institute medical treatment rather than surgical*. As I recently explained⁹ all the symptoms which yield to internal treatment are presented, indeed, with maximum intensity in the climacteric variety. These symptoms are the lack of comprehensive goiter, the transitory nature of the attack and the efficacy of psychotherapeutic agents.

Strumitis in the Menopause

As a continuation of *climacteric hyperthyroidism* let me mention another thyroid symptom which occurs at times during the critical years—I refer to *strumitis*, and women with goiter suffer rather frequently from inflammation of the tumor, either through

⁸Aschner: Op. cit., note (31), page 255.

⁹Marañón: Traitement de la maladie de Basedow. Revue de Médecine, 1924.

the influence of general infectious processes, or through the simple circulatory disturbance inherent in genital imbalance, such as puberty, menstruation, pregnancy and menopause. (Berard.¹⁰) I have seen two very typical cases of acute strumitis. Besides the local symptoms of induration and hypertrophy and pain in the gland radiating to the neck and shoulders, along with fever they showed the syndrome of acute hyperthyroidism, rapid loss of weight, tachycardia, retraction of the upper lid, tremor and nervousness. In one of these cases, a woman of thirty-one, the phenomenon coincided with abrupt suspension of the menses on the second day because of a severe fright, and lasted eight to ten days. The second case was that of a woman of forty-six in whom the strumitis appeared without apparent cause, in full health and during her natural menopause when, for the second time, the menses failed to appear. Two months later she was much relieved of the thyroid inflammation but the hyperthyroid manifestations had not disappeared.

Climacteric Myxedema

The *hypothyroid reaction* in the critical age is as we know much less frequent than the hyperfunctional.

[Relative to the symptoms of climacteric myxedema, my impression is that such cases are not so rare in that region of the United States about the Great Lakes. They are rarely recognized by the doctor as climacteric but are treated rather as nervous prostrations, neurasthenics, etc., etc. In addition to all of the symptoms here described there is seen also loss of memory. This, like the others, may be mild or severe, but is so marked in some cases as to cause the patient to fear that she is losing her mind. I have never, however, seen a state of true, premature senile dementia develop.—C. C.]

When it does occur, the hypothyroid symptoms predominate in such a way that in certain cases we may speak of true states of *climacteric myxedema*. This syndrome may appear in three ways. 1. In most cases *these women have been hypothyroid since youth*, as I have said on page 48. Deusch¹¹ calls attention

¹⁰Berard: Corps thyroïde. Paris, 1908.

¹¹Deusch: Op. cit., note (46), page 48.

to the same thing. While this hypothyroidism has been more or less tolerated during life, *the menopause, which appears early, accentuates it and converts it into a true myxedema.* Case 41 (page 176) is a typical example of this variety. 2. *In women who have previously been hypothyroid the beginning of the crisis is accompanied by hyperthyroid symptoms which are more or less intense and numerous, such as tachycardia, palpitation and nervousness. These symptoms are intermingled with the regular hypothyroid symptoms for some time giving rise to the clearest picture of so-called thyroid instability.* The hyperthyroid manifestations are generally transitory, disappearing later as the pure myxedematous picture emerges in a complete, aggravated form. 3. *In women whose temperament is usually hyperthyroid—even frankly and pathologically hyperthyroid throughout life—after a passing exaltation of the hyperthyroid manifestations these may rapidly lessen and the clinical picture be transferred into that of myxedema, post-basedowian myxedema.*

The symptoms of this state are those of *ordinary myxedema.* The woman becomes flabby. Her skin is thick and wrinkled. Her voice is hoarse. She becomes very sensitive to cold through a defective peripheral circulatory system. A deep apathy invades her and perhaps a profound somnolence. Her hair falls out. She complains of headache and constipation, of digestive upsets which are frequently due to a hypochlorhydria.¹² Hearing is less acute and eczematous affections of the skin are rather frequent. According to Deusch the climacteric “suffocations” are apt to be less intense. But in some cases I have seen this was not so, their violence contrasting rather with the feebleness of the rest of the clinical picture. The intensity, the depth of the morphologic and psychic transformation which the woman experiences at times, and which makes her appear a stranger to her intimate friends when they have not seen her for some time, can only be compared to the speed with which this all disappears, when, if diagnosed in time, she is subjected to thyroid therapy.

Although “climacteric myxedema” is not very frequent, I believe the general practitioner’s attention should be called to it.

¹²In one of Deusch’s cases, this hypochlorhydria not only was cured but was transformed into hyperchlorhydria through thyroid therapy. This case coincides with those I reported elsewhere.

I have seen typical myxedemas which were erroneously considered for years as cardiac cases (Case 41, page 176) or, more frequently as nephritides which they closely resemble. This mistake is the more easily made since myxedema often coincides with a slight



Fig. 15.—Climacteric myxedema. (Personal case.)

albuminuria. In recent years, along with my collaborators Peralbo, Pardo and Raguz I have been particularly interested in these nephritic changes in the myxedematous and have come to the conclusion that the myxedema produces secondary renal changes which are amenable to the same treatment as the myxe-

dema itself. Hence in interpreting the renal episode one should not forget the causal process. Of many such cases which we have recognized the following may be quoted:

CASE 65.—S. de B.—Thirty-nine years old. Menses always scanty; tendency to put on weight; intensely sensitive to cold—that is, usual mild, thyroid insufficiency. On reaching midlife, she developed edema of the eyelids and face which took on the broad, pale aspect of the nephritic facies. She became apathetic and slow in all her manifestations. Provisional *diagnosis of nephritis*. Urinalysis showed 50 cg. albumin and a not gravely disturbed elimination. This confirmed the diagnosis. But her physician was surprised during the following months by the rebelliousness of the swelling and albuminuria and in spite of a milk diet. I then saw her. A careful examination allowed me to change the diagnosis to that of *climacteric myxedema*. She was given *thyroid and ovarian treatment whereupon the swellings went down quickly and the albumin in the urine disappeared*.¹⁴

Mild Thyroid Insufficiency. Obesity.

In general thyroid insufficiency is manifested much more frequently through symptoms indicative of a slight insufficiency rather than by myxedema properly speaking—which is the expression of a serious lack of secretion. Among these symptoms of lesser thyroid function is obesity. In a previous chapter I said that the obesity which frequently appears in this age is not apt to present hypothyroid characters, at least in the majority of cases. With or without obesity various other symptoms of mild thyroid insufficiency more or less pronounced and well-known appear. These are, fugitive edemas, especially palpebral, sensations of cold, apathy, hemicrania, constipation, the eyebrow sign—that is, absence of the outer half of the eyebrow—and so forth. The patient shown in Fig. 15 is an example of this incomplete thyroid insufficiency of the critical age. The results of opotherapy in these cases are likely to be excellent.

¹⁴In the cases recognized recently and which I shall publish later, the renal function was determined. This was not done here but otherwise this case is very typical of myxedematous nephritis.

Thyroid Instability. Fluctuating Type

I have said that it is in the menopause that the states of so-called thyroid instability reach their clearest clinical expression. This is especially true of the cases in which clear hyperthyroid symptoms are mixed with clear hypothyroid symptoms. But, I insist upon this, the hyperthyroid predominate.

L. Levi¹⁵ has recently described the production in states of thyroid instability of *multiple fluctuations* in different and distinct parts of the body. These are produced by a localization of the angioneurotic attacks from which the patients frequently suffer. Such fluctuations are manifested by various symptoms, dependent on their localization, which deceive the physician by their disparity and apparent lack of dependence upon a common cause. For example, in a case he describes there occurred successively, *loss of memory, ovaritis* which required operation, *parotitis, thyroiditis and painful attacks in the gall bladder*. All this was relieved by thyroid therapy in small doses. I have seen some cases of menopausal women who reminded me of this description, hence I call attention to it. Probably in the same category should be included Mussio Fournier's case.¹⁶ This was that of a woman in the critical age with predominately hypothyroid symptoms in whom a painful facial paralysis occurred. Because of its form of presentation and because of the general clinical picture, the writer assumed it was due to a fluctuating state of thyroid origin localized in the facial nerve.

Suprarenal Symptoms

Suprarenal pathology properly speaking has very little relation to the climacteric. The *hypofunctional syndromes*, Addison's disease especially, are always rare, and, on the other hand, have no special relation to the climacteric although this disease is frequently associated with disturbances due to genital insufficiency in youth.¹⁷ Certain *melanodermic syndromes*, which we

¹⁵Leopold-Levi: Op. cit., note (19), page 184.

¹⁶Mussio Fournier: Parálisis en una hipotiroidea. Revista Médica del Uruguay, 1917.

¹⁷See Marañón: Contribución al estudio de los síndromes pluriglandulares, Revista Clínica de Madrid, 1913.

shall study later, do not appear to have, as was formerly supposed, any relation to hypoadrenal melanoderma.

In regard to *hyperfunctional* or *hypersuprarenal syndromes*, I have already said that they do not have at present sufficient clinical reality for us to recognize them. Nevertheless, as I said on page 54, perhaps it is not so fanciful after all to consider states of hypertension and hyperglycemia or glycosuria, occurring so frequently in this age, as the consequence of a *medullary hyperfunction* of these glands. At least it is very possible that this factor takes part in the mechanism of its production, if not as sole cause as one of the coadjuvant pathogenic elements.

Another group of climacteric symptoms until recently related to *hyperplasia of the suprarenal cortex* is that comprising virilism, hirsutism, sexual inversion, and so forth. But as this matter is now in the very midst of controversy, I prefer to study these among the genital symptoms, without deciding their pathogenesis.

Hypophyseal Symptoms

The hypophyseal symptomatology is also very unsettled in the climacteric. I have spoken of cases of *acromegaly* (page 72) of *hypophyseal insufficiency* (page 65), of *diabetes insipidus* (page 68), of *localized adiposities, especially on the abdomen* (page 243) and of *hypophyseal cachexia* (page 254). I have also mentioned the possibility of a hypopituitary factor intervening in the pathogenesis of *localized lipomatoses* (page 247) in *Dercum's disease* (page 248) and in *Barraquer-Simon's disease* (page 250).

Sexual Symptoms. Climacteric Sexual Inversions

Here I do not refer to genital symptoms in the usual gynecologic sense, which have been amply treated in Chapter X, but to the genital disturbances directly dependent upon endocrine upsets which I therefore prefer to call "*sexual*."

The most interesting are those related to the revivification of the masculine sex characteristics. As I have already explained in Chapter XIV, every organism bears, besides the marked characters of its own sex, the characters of the opposite sex submerged and dominated by the vigor of the former. But when, through disease or surgical intervention or physiologic involu-

tion, the function of the genital gland is annuled, then, lacking the curb of that internal secretion, the heterosexual characters revive and make their appearance. This gives rise to somatic or functional states, alone or alternating, of sexual inversion or bisexualism. On page 57 I considered whether this revivification of opposite sex characters is related to hyperplasia of the suprarenal cortex or depends solely upon the ovarian extinction. Here that problem does not concern us, but rather the clinical fact. And the clinical fact teaches, indeed, that these inversive states of varying complexity and intensity¹⁸ are very frequent in the menopause.

As I have said, the inversion may be limited to a single anatomic sign; it may include several such signs accompanied by psychic inversion, or may be reduced to this last alone. All varieties of the process are found, and it is convenient to include them all under a common concept in order to simplify the subject and avoid the complicated terminology which has accumulated about this question. Let us call it then *sexual inversion*, in women, virilism. Within this group we shall study the following varieties.¹⁹

1. *Total inversion, total virilism.*—In some cases the inversive sexual tendency refers to psychologic characters, including the sexual instinct and the morphologic symptoms. I have already explained on page 192 that this coincidence, contrary to the belief of Freud and other psychologists, is in my opinion much more frequent than is supposed. Here is one of my cases which is very striking.

CASE 66.—H. de L. Forty-one years old. American. Constitution always strong; decided character but apparently nothing inversive about it. From her youth she was known for her excesses, generally related to sexual subjects. She married but

¹⁸I should call attention to the fact that this virilism, or tendency to heterosexual transformation in the climacteric female, does not occur solely in the human species. It is observed in various animal species. For example in old hinds, horns like those of the buck appear. Hens past the age of reproduction develop spurs like those of the cock. Changes in the color and disposition of the plumage has been reported as occurring in the old female turkey, mandarin duck, and pheasant. These changes sometimes exactly resemble the external characteristics of the respective males.

¹⁹This classification, naturally, may be applied to all cases of virilism, not only to these of the climacteric.

was soon separated from her husband. A little later, at her thirty-fifth year, her public and scandalous relations with other women began. She was considered a great pervert. But when examined from the endocrine point of view a parallel somatic transformation was observed in her, coinciding with premature genital insufficiency which soon was complete and definite. She became corpulent, her voice heavy. Marked down appeared on the face, neck and trunk, and the mammae atrophied. She herself perceived the change in her character in the direction of a greater decisiveness and also an increase in muscular strength. She confessed that from the first her relations with man had not been pleasing while, on the other hand, women attracted her irresistibly.

2. *Purely psychic inversion, psychic virilism*, that is to say, not accompanied by somatic changes. I have already referred to this type which sometimes is a pure change in instinct (page 215), and other times is a true psychopathy (page 218).

3. *Purely somatic inversion, somatic virilism*. This is the most common type in the climacteric. In it the virile tendency is limited to one or more anatomic signs while the psychic and the instincts remain within the feminine standard. In the majority of women, who on reaching this age present the virile transformation, the signs more or less marked are increase of corpulency, appearance of down, and lowering of the voice, while none of her femininity is lost.

Within this type, the most marked and frequent manifestation, *at times the only one, is hypertrichosis*. This may be divided into three grades. In the first it is limited to a slight appearance of fine down or of coarse, isolated piliary growth on the elected sites, chiefly the upper lip, chin, beneath the chin, the sternal region, forearms and legs, and the midline of the abdomen. This yields readily to cosmetic remedies. In the second grade the hair is more abundant and coarse, now constituting an anomaly and attracting attention but still limited to the same regions. In the third grade the piliary growth reaches its maximum both in vigor and thickness and in its dispersion over the whole trunk and chin region. In short, these are the *cases of monstrosity*.

Pliny observed this phenomenon and related it to premature menopause, as cited by Le Double and F. Houssay.²⁰

At times the hypertrichosis and perhaps the other signs of virilism are combined with a melanoderma, giving rise to the syndrome which I described for the first time under the name "bronzed virilism."

Bronzed Virilism

I have described this syndrome elsewhere in detail. Here I shall give only a summary of its clinical characters. *In such cases the women acquire the somatic and functional signs of virilism, such as plethoric aspect, even true obesity, hypertension and abundant, even monstrous, ectopic hair. With these are combined a diffuse melanoderma, generally total, with darkly pigmented spots like those appearing in Addison's disease. The color of the skin is, indeed, like that which is presented in suprarenal insufficiency. But in place of finding the other hyposuprarenal symptoms, asthenia and increase of weight, manifestations are found which makes one think rather of a hypersuprarenal origin.*

I have seen four typical cases of this affection whose pathogenetic explanation leads us to excessively hypothetic fields. Later we shall see that genital upsets, of themselves, may give rise to these pigmentary states. Sometimes these are very extensive coinciding in this case with somatic sexual inversion. The type of pigmentation in such cases especially recalls that of bronzed diabetes.

Climacteric Pluriglandular Sclerosis. Premature Senility

Climacteric pluriglandular sclerosis is very interesting. A certain number of women of *asthenic habit*, with nervous, digestive and other complaints inherent in this age, on reaching the critical age acquire a *premature senile* morphology with premature meno-

²⁰(a) Le Double and F. Houssay: *Les Velus*, Paris, 1912. The necessity of distributing the study of sexual inversion over several chapters has made it necessary to dispense with the bibliography on it. Besides the works mentioned on page 57, note 14, 15, and p. 58, note 16, 17.

(b) Quinby: *Pseudohermaphroditism; Remarks on Abnormal Function of Endocrine Glands*. Bull. Johns Hopkins Hosp., 1916.

(c) Tuffier: *Le virilisme surrenale*, Rev. de therap. med. chirug., 1914.

(d) Swindle: *The Accessory Chromosome in the Frog Possessing Marked Hermaphroditic Tendencies*, Biolog. Bull., 1916.

(e) Goldschmidt: *Intersexuality and the Endocrine Aspect of Sex*, Endocrinology, 1917.

pause. (Page 105.) This is particularly true if they have had several children, and asthenic women are apt to be very prolific. This premature senile aspect is initiated through the sclerotic change in the thyroid, suprarenal, ovarian and hypophyseal glands. This condition corresponds to the early descriptions by Claude and Gougerot of *pluriglandular insufficiency*,²¹ to many of the cases of *genitodystrophia geroderma* reported by Rummo and Ferranni²² and to those attributed by Wiesel²³ to *conjunctive diathesis*. In my opinion, the so-called asthenic habit, commonly recognized by clinicians and which therefore need not be described here, is a general insufficiency of the endocrine system either through a congenital debility or through a sclerotic change perhaps related to some such condition as syphilis or tuberculosis in the forebears.

The endocrine functions, in so far as they impel morphologic development and the maintenance of visceral and muscular tone, can easily be conceived as causing the general deficiency in development and the visceral hypertonia which characterize the asthenic habit. The clinic, however, proves the frequency with which these asthenic subjects present endocrine symptoms, those of hyperthyroidism,²⁴ hypothyroidism, suprarenal insufficiency and so forth. The clinic further proves, on the other hand, the favorable modification of asthenic symptoms through well-directed opotherapeutic treatment. Admitting a previous debility of the endocrine system in asthenic women, it is recognized that this debility is accentuated when in the course of life there occur those causes which usually conduce to functional quenching of these organs; we refer here to such things as chronic infections (principally tuberculosis and syphilis), miserable and unhygienic lives, and especially oft-repeated pregnancies and

²¹Claude and Gougerot: Les syndromes d'insuffisance pluriglandulaire; leur place en nosographie, Rev. de Med., 1908.

²²Rummo and Ferranini: Geroderma genitodistrofica. Riforma Medica, 1897.

²³Wiesel: Die Bindegewebendiathese als Ursachs multiglanduläre Störungen, in Lewandowsky, Handbuch der Neurologie, Berlin, 1913, iv.

²⁴See Novoa Santos: Astenia constitucional y tireosis. Revista Clinica de Madrid, 1914, ii. In this interesting article the author emphasizes the importance of the asthenic constitution in the production of hyperthyroid states. It is true that many asthenics are, indeed, hyperthyroids, more or less masked. But cases are also found wherein there are hypothyroid or hypoadrenaline symptoms.

lactations.²⁵ *Both classes of factors, the congenital and the acquired on reaching the menopause bring about a state of premature senility which, as we have seen, may be considered a pluriglandular insufficiency.*

Such women present at once the general somatic signs of asthenia, thinness, graceful skeletal lines, long flat thorax, acute sternal angle, floating tenth rib, cardiovascular hypoplasia, weak musculature, general visceral ptosis. Besides these there are *the functional symptoms inherent to this state.* (a) Circulatory instability characterized by palpitations, hypotension, etc. (b) General nervous manifestations such as dizziness, asthenia, psychasthenia, algias, etc. (c) Vague and persistent digestive upsets, particularly flatulency, aerophagia, colitis and constipation. (d) Finally, endocrine symptoms, pluriglandular as in premature senility; wrinkled facies, sallow and freckled skin, lenticular melanodermic spots on the backs of the hands being especially typical; teeth movable and carious; jaws atrophied; hair intensely white; mammae atrophied; pubic hair straight; low basal metabolism. Case 31, page 105, is a typical example of this state.

As I indicated there, in some of these cases, in spite of the general endocrine debility the reproductive function may be very active. Such women are prolific and this very fact contributes to the final syndrome of senility.

²⁵ "The work of bearing, shortens youth; too frequent harvests exhaust the field." (Ovid. *Artis Amatoriae*, book III).

CHAPTER XIX

DIGESTIVE SYMPTOMS

Outline

Digestive disturbances of the climacteric	(a)	{ Hyperchlorhydria
		{ Hypochlorhydria
		{ Flatulent dyspepsia
	(b)	{ Bulimia
		{ Alcoholism
	(c)	{ Constipation
		{ Diarrhea, intestinal colic
		{ Colitis
	(d)	Hemorrhages of the digestive apparatus
	(e)	Pharyngeal and esophageal spasms
	(f)	{ Climacteric icterus
		{ Cholelithiasis
	(g)	Mikulicz' disease

Hyperchlorhydria and Climacteric

Among the different gastric disturbances appearing in this age and connected with the neuroendocrine crisis perhaps those most frequently observed are the following: hyperchlorhydria and vague dyspeptic disturbances, with or without aerophagia but with a predominance of the complaints caused by the gaseous repletion in the abdomen which we may continue to designate as *flatulent dyspepsia*. Hyperchlorhydria has been pointed out by Elsner¹ as very frequent during the menstrual flow. It has often been observed in pregnancy. Kehner² and Hernando³ have described this same condition in women with ovarian disease. *It is frequently found in the menopause generally in a transitory form with the characteristics of nervous hyperchlorhydria, according*

¹Elsner: Der Einfluss der Menstruation auf die Tätigkeit des Magens, Archiv. f. Verdauungskrankh., v, page 467.

²Kehrer: Die physiologischen und pathologischen Beziehungen der weiblichen Sexualorgane zum Tractus intestinalis, Berlin, 1905.

³Hernando: Enfermedades del estomago, in Manual de Medicina interna, by Hernando and Maranon, 1916, i.

to my experience and that of other writers, Vinay,⁴ Dalché,⁵ and Robin (cited by Vinay). I record a case at length because of the complete dependence which was observed in it between the menstrual suppression and the gastric disorder.

CASE 67.—Woman of forty-two years, menses always scanty, although regular; without children. *No previous gastric disturbance.* Without previous menstrual or important general disturbances. The menses skipped one month and *immediately she began to complain of suffocations, tachycardia, palpitations and great hyperchlorhydric distress; acidity, burning sensation, the epigastrium became painful later, very acid vomit, etc.* The symptoms were alleviated by an alkaline diet, ovarian extract and belladonna. During the two following months menstruation appeared and the gastric complaints were absent. *At the third month, amenorrhea again and reappearance of circulatory and gastric disturbances.* Two years later I again saw her. Definite menopause and perfect digestion.

Elsner attributes menstrual hyperchlorhydria to a hyperemia of the gastric mucosa. Vinay gives the same explanation for *menopausal hyperchlorhydria*, as does Robin who published a case very similar to the one just given. In my judgment, *hyperthyroidism, so common during the menopausal crisis, must play an important part in climacteric hyperchlorhydria.* I have demonstrated⁶ that, in many cases, hyperthyroidism produces an intense vagotonic reaction which manifests itself, aside from other symptoms, by a hyperchlorhydria of nervous type which readily yields to antithyroid remedies. This is true of a great many menopausal women with hyperchlorhydria. Moreover, in these it is an easy matter to find a great predominance of hyperthyroid symptoms; this demonstrates the importance of this climacteric factor in the production of the gastric disturbances. Of the many cases I have seen, I shall cite two examples.

⁴Vinay: Op. cit., note (12), page 19.

⁵Dalché: Troubles gastriques de la ménopause, Bull. de Therap., 1900.

⁶Marañón: Op. cit., note (5), page 266. With some exceptions, the majority of writers now accept my hyperthyroid explanation of these hyperchlorhydrias. According to Escudero (Dispepsia tiroidea. Revista Española de Medicina y Cirugía, Barcelona, 1920, page 355), the thyroid disturbance may give rise primarily to impairment of gastric motility to which the changes in secretion may be attributed.

CASE 68.—A. C. Forty-seven years old. Always well until six months ago, when menstrual disturbances began, and with them *a clear hyperthyroid syndrome*; loss of 10 kilos in weight in that time; tremor, tachycardia exophthalmos, insomnia and poor emotional control. Three months later, *a severe attack of hyperchlorhydria* with epigastric burning and pain, copious and very acid vomit. Ovarian and antithyroid remedies alleviated all the symptoms including the hyperchlorhydria. The menses returned and during the period the hyperchlorhydria disappeared almost entirely.

CASE 69.—S. de H. Forty-one years old. Goitrous family. Following one of her labors she had a typical and intense hyperthyroidism. This was much improved by surgical intervention. Now, coinciding with the critical age, *the hyperthyroid symptoms returned*, tremor, tachycardia, emotionalism and infarct of the thyroid region. With these there appeared *hyperchlorhydric complaints*, sensations of "heart burn" and sometimes acid emesis which alkalis temporarily alleviated. I do not know the result of my treatment which was antithyroid serum, ovarian extract and belladonna.

Cases of Hypochlorhydria

Hernando⁷ has described hypochlorhydric states in women with ovarian insufficiency, but these were cases of premature menopause or of castrated women, that is to say, women in whom the climacteric crisis, and therefore the hyperthyroidism, is not apt to reach the completeness that it does in the menopause occurring at the physiologic time. But even in these, it is certain there may be found complaints of hypochlorhydric type, as occur in advanced hyperthyroidism itself with symptoms of asthenia. (Wolpe.) If these symptoms predominate in the crisis, then hypochlorhydric disturbances may be presented. A hypothyroid reaction, observed in some menopausal women, would have the same effect, since Lockwood, Hernando and Deusch⁸ have seen hypochlorhydria in hypothyroidism.

⁷Hernando: Las llamadas alternaciones nerviosas y funcionales del estomago. *Anales de la Acad. Med.-Quirurg.*, 1914-1915.

⁸Deusch: *Op. cit.*, note (46), page 48. In the preceding chapter I commented upon these articles.

Flatulent Dyspepsia in the Critical Age. Aërophagy

Flatulent dyspepsia is also very frequent. Many menopausal women complain of such symptoms as troublesome digestion, with sensation of intense fullness, meteorism and eructations. These disturbances do not appear to correspond to a marked secretory change as they may be present with normal acidity, with mild hyperchlorhydria or, more frequently, with more or less marked hypochlorhydria. In other cases the gastric picture remains the same, figures above or below normal being found, according to circumstances as Yagüe described in many neuropathics. No doubt neuropathic changes, such as aërophagy, and disturbances of intestinal motility, have an influence in the production of this flatulent dyspepsia. I shall speak of these changes presently. The dyspepsia frequently coincides with *the development* of abdominal fat in great excess both extra- and intra-abdominally which perhaps intervenes in a mechanical way in the pathogenesis of dyspeptic symptomatology.

In some women, *especially in aërophagic neurotics, frequent in this age, meteorism becomes very intense*, producing extraordinary symptoms at times. The abdomen becomes very large, causing intense oppression, dyspnea, tachycardia, even palpitations and predisposition to suffocations. These women at times are obliged to eruct repeatedly and noisily in order to relieve their momentary distress. They may have to loosen the corsets. Kisch,⁹ Wagner,¹⁰ and other writers have cited cases in which the meteorism was so exaggerated and so permanent that it gave rise to a false diagnosis of pregnancy or of abdominal tumors.

I have already indicated in the proper chapter, the influence these disturbances may have on the appearance of grave circulatory symptoms which sometimes occur in climacteric women. I would add here that the opposite may occur. That is, initial de-compensations may be manifested only through these dyspeptic complaints for a long time.

Pathologic Appetite

A symptom which I have seen repeatedly in many climacteric women, and to which writers do not call attention, is *bulimia*.

⁹Kisch: Op. cit., note (13) page 19.

¹⁰Wagner: Op. cit., note (28), page 131.

Indeed, I have observed with a certain frequency *that women who have had normal appetites, upon reaching the menopause give way to excesses in eating*, with unusual avidity and even to true gluttony. Sometimes this symptom makes one think of the possibility of diabetes which later examination does not confirm.

I might cite various cases illustrative of this phenomenon. The intense and disordered appetite may influence the appearance of the digestive upsets we have just been considering, such as metabolic disturbances, obesity and diabetes.

Likewise *a tendency, coincident with menstrual cessation, to the abuse of alcoholic beverages* has been observed. Women who have been temperate, with no social or organic reason for such indulgence, now give way to alcoholism to a greater or less extent. Certain of these cases, like some cases of pathologic bulimia, really belong to the domain of psychiatry. But they are mentioned here only because of their relation to gastric disturbances. Here is a typical case.

CASE 70.—B. A. Forty-two years old. Cuban. Menses regular. Married, with two children. Of very good dietetic habits. Usually she drank only a glass of white wine with her breakfast. Those about her began to notice that she lost weight without apparent cause and grew to be very nervous and excitable. After two months observation during which I tried every remedy, I came to the suspicion and later conviction that she was an alcoholic because of her tremor, psychic symptoms, and other indications of a domestic nature. *When questioned persistently she at last confessed that she had been drinking secretly for some time two or three bottles of white wine daily.* She could give no reason for this craving and had drunk the wine between meals to conceal her act from the family. It is odd that she had had no attacks of acute alcoholism. *Three months later menstrual disturbances began* which have lasted up to the present. Suppression of the alcohol and some tonic injections cured her in due time.

Gallard (cited by Vinay¹¹) has reported similar cases and I have seen several others, less typical, however.

¹¹Vinay: Op. cit., note (12), page 19.

Climacteric Constipation

From the time of Hippocrates much importance has been given to the intestinal disturbances of the climacteric. Tilt found diarrhea in 72 per cent of the menopausal women observed by him.¹² Other writers, Kisch, Vinay, Culbertson, Wagner (so often cited), Boerner¹³ and Gallichan¹⁴ give constipation as the most frequent symptom. According to my experience, *of 103 menopausal women in whom I sought these symptoms, 35 had no change in intestinal function, 33 per cent. In 22, the menopause had produced constipation, 21 per cent. In 26 former constipation was increased with the menopause, 25 per cent and in 19 there was diarrhea, 18 per cent.* I give to these figures only the relative importance which I give to the statistics of others, since I am thoroughly convinced that the factors which intervene in their make-up are somewhat subject to error. However, *the indubitable fact remains of the frequency with which constipation appears or is exacerbated in the critical age.*

This constipation has no special characteristic other than its persistency, its resistance to remedies, and the part it takes at times in the production of abdominal meteorism, which I pointed out before, with its reflex intervention on the respiratory, circulatory, and similar menopausal symptoms. *Usually it is an endurable complaint, to which the woman pays scarcely any attention.* Consequently the physician must inquire specifically about it.

Climacteric Diarrhea and Intestinal Colic

On the other hand, *diarrhea, being less frequent, is of much more pathologic importance.* It is presented either in the form of continuous diarrheas or, more frequently, in the form of diarrheic attacks which last from some hours to a day and are produced by different causes, very frequently psychic. They are common in women with hyperthyroid reaction (see the previous chapter). Occasionally they are accompanied by noises in the abdomen, at times so loud that they are a torment to the patient.

¹²Tilt: Op. cit., note (10), page 102.

¹³Boerner: Die Wechseljahre der Frau, Stuttgart, 1886.

¹⁴Gallichan: Op. cit., note (37), page 21.

In one of my cases this phenomenon obliged the woman to withdraw, for a time, from social life, to which she had been devoted. Less often colicky pains appear. Finally, *climacteric diarrhea* presents the characteristic of refusing to yield to the pharmacologic remedies. *Painful colic* at times may be very striking, as in the following case:

CASE 71.—M. de M. R. Forty-five years old; without important antecedents; strong constitution; multipara; menses regular. Some months ago menstrual disturbances began, accompanied by very painful *intestinal colic*, the griping lasting, sometimes, several hours; and the attack ending by the expulsion of gases and liquid stools. These symptoms were presented, chiefly, during the menstrual days. Intestinal examination disclosed nothing of particular interest. I do not know the result of the treatment, diet and ovarian extract.

The influence of emotional states on climacteric diarrhea is very interesting. It is so marked that these may be included frequently in the group of emotional diarrheas. This is seen in the following case:

CASE 72.—P. de la M. More than forty years old. Of very haphazard and light sexual life in her youth, she lived for the last ten years a rather tranquil life with a man of calm nature. In this age, coinciding no doubt with the first climacteric changes, she felt again impelled to a life of greater amorous activity and went by night to a restaurant where she met a young man of whom she was enamoured. A few days later she had an assignation with him. She related later, with desperation, that the two times on which she was on the point of obtaining the object of her passion, the organic commotion had been so violent, that a copious diarrhea had occurred. This woman had a rather fat neck and was very nervous. But I noted no other hyperthyroid signs.

This case may be included among the *conjugal diarrheas* which Hernando correctly likens to thyroid diarrheas. The following case is also very interesting as it concerns a woman habitually constipated.

CASE 73.—A woman in full menopause, somewhat early (forty-two years), very emotional since the beginning of the climacteric, always constipated. Her husband, a soldier, had gone to war. News from Africa was delayed and her moments of anxiety, as upon hearing any one speak of a new battle, *were marked by attacks of repeated diarrhea*. She presented severe suffocation, intense vasomotor irritability, tachycardia, palpitation, and marked nervousness.

In some menopausal women *the diarrhea presents itself in the days wherein the menstrual period should occur*. Especially in these cases, but also in others, its appearance is apt to coincide with the alleviation of the symptoms of circulatory origin. Therefore some writers, even Hippocrates, and many women, empirically and correctly attribute to it a vicarious significance, useful to the organism.

Diarrhea may appear very early in menopausal symptomatology. In some cases it announces the advent of the critical age, before any other signs. (Singer.¹⁵)

Pathogenesis of the Intestinal Disturbances of the Climacteric

The pathogenic interpretation of these intestinal symptoms—formerly attributed to well-recognized abdominal congestion, can be made much more precise from the modern endocrine point of view. *Almost always these symptoms appear in cases suffering from disturbances of intestinal innervation, of intestinal neurotony* (Guillaume¹⁶) linked with the abdominal hormonal influences, so frequent in this age.

These hormonal influences may be the following: on one side, *the internal thyroid secretion acts by increasing the intestinal tone and the peristaltic movements*, as Deusch¹⁷ has demonstrated in the intestine of animals and in man. This action has been observed through x-rays when the subjects were given intravenous injections of thyroid preparations. This data coincides with the classic belief to which we all have contributed that in thyroid

¹⁵Singer: Op. cit., note (28), page 131.

¹⁶Guillaume: La constipation et la stase intestinales chroniques, Bull. Med. Paris, April, 1923.

¹⁷Deusch: Die thyreogene Constipation. München. med. Wehnschr., 1923, lxx.

insufficiency one of the usual symptoms is constipation. This type of constipation is readily cured, especially in children, by corresponding opotherapy,¹⁸ according to my experience. Therefore, in climacteric women of hypothyroid tendency, this same explanation may be invoked (Deusch).

On the other hand, *adrenalin has as one of its fundamental actions, that of paralyzing the muscular contraction of the intestine.*¹⁹ Thus one may advance the hypothesis that the supposed hyperadrenalinemia of the climacteric may give rise to a state of *hypersympathicotonia*, which acts on the constipation. Culbertson²⁰ brings in support of this hypothesis, the fact which I, too, have confirmed, that the very constipated menopausal women are apt to be more hypertensive.

Finally, it is possible *that the hypophyseal insufficiency, not rare in this age, also acts on the intestinal innervation*, since peristaltic action of hypophyseal extracts is known. This fact coincides with the observation I made concerning intestinal paresis in hypophyseal insufficiency as being quickly relieved by pituitrin.²¹

As for the diarrhea, it is, in my opinion, like the hyperchlorhydria before commented upon, a vagotonic diarrhea, linked almost always with the climacteric hyperthyroidism. Just as constipation coincides with hypertension, diarrhea is apt to coincide with the accentuation of the hyperthyroid symptoms so frequent in the critical age.

Recently Hernando²² studied the frequency with which diarrhea is presented in hyperthyroidism, even in its attenuated forms, with the same characteristics assigned to climacteric diar-

¹⁸In this connection see (a) Levi et Rothschild. Op. cit., note (1), page 33.

(b) Minoret: Corps thyroïd et intestin. These de Paris, 1911. This writer attributes certain constipations of pregnancy to hypothyroidism.

(c) Oliver Pascual: Sobre dos casos de estrenimiento de origen tiroideo. Archivos de Med. Cirug. y Especial, Madrid, 1922, vi. Relying on a study of basal metabolism, he believes that the number of cases of hypothyroid constipation is really larger than has been thought.

¹⁹(a) Hoskins: The Asthenic Effect of Epinephrin Upon Intestine, Am. Jour. Physiol., 1912.

(b) Hoskins and McClure: The Comparative Sensitiveness of Blood Pressure and Intestinal Peristalsis to Epinephrin, Am. Jour. Physiol., 1912. Many other writers have confirmed these results which are now classic.

²⁰Culbertson: Op. cit., note (28), page 21.

²¹In the opinion of many writers this peristaltic action of pituitrin, like its many other actions, is merely a pharmacologic one, without any physiologic powers. I do not weary of repeating my disagreement with this view, contrary to all biologic philosophy. In the same way we might say that insulin acts only pharmacologically and not in a physiologic manner.

²²Hernando: Op. cit., note (16b), page 266.

rhea. These characteristics are independence of dietetic causes, dependence on psychic causes, especially emotions, and accessional presentation. *According to my experience with 937 cases of hyperthyroidism in all its forms, diarrhea was present in 251 cases, 27 per cent.* In a few, it was so severe that it endangered the patient's life.²³ I have no complete data on the coincidence of these cases of hyperthyroid diarrhea with the critical age. Nevertheless in many of them this coincidence existed.

Hernando discusses the pathogenesis of *hyperthyroid diarrhea* which, as we have just seen, can be identified with climacteric diarrhea. He rightly rejects the hypothesis that it may be due to a hypochlorhydria, a gastrogenic diarrhea, since, as we know, in hyperthyroidism and in the menopause, hyperchlorhydria is most frequent. He admits a vagotonic origin for the intestinal disturbance, a hypothesis perfectly in accord with intestinal physiology and with thyroid physiology; and one which, moreover, gives a reason for the emotional origin of many of these diarrheas. It also explains the coincidence of the diarrhea with hyperchlorhydria, since we know that both may have the same origin—*vagotonia*. *It is impossible to overstress the necessity of excluding the existence of organic causes capable of producing these intestinal disorders before resorting to the less transcendent diagnosis of climacteric.* Indeed, aside from grave lesions of the digestive tract, such as ulcers or cancer or general processes with digestive symptomatology like uremia, there are certainly other causes of nonendocrine origin which may also produce these same intestinal disturbances. For example, among more common factors we find *mechanical constipation*, due to a displaced uterus or to genital or pelvic inflammations; also constipation and diarrhea of purely digestive origin related to the gastric symptoms studied above.

Membranous Enteritis and Appendicular Colic

Vinay,²⁴ Rankin²⁵ and others say they have often observed *mucomembranous enteritis*. It may be presented as a complica-

²³The cases seen since the publication of the first edition of this book, have reduced the proportion which was there given as 35 per cent.

²⁴Vinay: Op. cit., note (4), page 19.

²⁵Rankin: Op. cit., note (12), page 43.

tion, not as the direct cause. Let me note only that thyroid and suprarenal factors may intervene in its pathogenesis according to recent writers.

The same may be said of *appendicular colic* which Vinay has described in menopausal women. They are related, no doubt, on one side to the aforesaid disturbances of constipation and mucomembranous colitis; on the other, to the ovarian congestion, especially of the right ovary, frequent in the critical age. In previously inflamed ovaries this congestion may be very intense.²⁶ And, finally, they are related to the heightened nervousness of this age which exaggerates a painful phenomena.

Hemorrhages of the Digestive Tract in the Menopause

Various hemorrhages of the digestive tract may be presented in the climacteric woman. When considering *vicarious hemorrhages* (page 130) I spoke of the mechanism producing this phenomenon. Like the general phenomena, it is due to the circulatory plethora, caused by the absence of the menstrual flow and favored by the hypertension frequent in this age. Like all *local phenomena* such hemorrhage is due to the existence of an old lesion, hidden or manifest, in various organs of the body. This lesion gives rise to a point of least resistance and here the blood finds easy exit. Thus we see that old lesions, often unsuspected, in the gastric or intestinal mucosa give rise respectively to *hematemesis* or to *melenas*, which present themselves with or without periodic rhythm. I have also insisted on the caution with which one must avoid giving a benign prognosis to these hemorrhages merely because they are vicarious, since they may be related to grave lesions which have been concealed up to this time.

But in the lower intestinal tract *a variety of hemorrhage, due to hemorrhoids is presented, which we may accept, generally as benign, with the sole reservation of the possibility of rectal carcinoma*, as I said in Chapter X. Hence, when these hemorrhages are a little persistent, we must resort at once to proctoscopic examination. Cancer may be present in this region for some time without subjective complaint, local or general, which would cause one to think of so grave a diagnosis. Here is an example:

²⁶The close relationship between various affections of the adnexa and appendicitis is well known; see Wagner: Op. cit., note (28), page 131.

CASE 74.—M. de C. A. Always healthy. Obese in her youth, but much thinner as a result of very intense thyroid treatment. Menses regular. Two children. At forty-three she began to have copious menstrual hemorrhages. She lost some weight and she felt rather weak, which she attributed to the loss of blood. She presented no abdominal pain. Good appetite and good color. Three months later I saw her again and found her much thinner, somewhat sallow, and complaining of *bloody diarrheas*, to which she attributed her loss of weight. The menses had definitely disappeared. On abdominal palpation, to which up to then she had objected, a *swelling* the size of a large orange was found in the left side of the abdomen, in the iliac fossa, rather high and deep, slightly painful. Inguinal adenitis. Nothing was felt by rectal examination. I diagnosed this as cancer of the sigmoid flexure which had developed almost without symptomatology. The process followed a slow course, but at the end was very typical of cancer, the patient dying two months later of intestinal obstruction.

Furthermore, according to my experience, in some cases vicarious hemorrhage from the rectum may make manifest a *syphilitic ulcerous lesion*. But with the exception of such rare possibilities, rectal hemorrhage, of red blood, arises from common hemorrhoids. The bleeding is more or less copious, having at times a menstrual-like character and all the appearance of a true *rectal menstruation*. Here is a typical case:

CASE 75.—Woman of forty-five years, strong, sanguine, constipated, with several hemorrhoidal attacks in her life. The menopause had developed sixteen months before with much distress; great hypertension. At the onset she had various menstrual irregularities; then *two months of amenorrhea*, and *five months later a hemorrhoidal hemorrhage of two days' duration*, rather copious, during the very days she should have menstruated. A year later she was well. The menses and the intestinal hemorrhage have both disappeared.

Pharyngeal and Esophageal Spasms

Textbooks do not mention a neurotic *affection of the digestive tract which is very frequent, in my judgment, in the climacteric*

age, pharyngeal and esophageal spasms. These spasms, which women of hysteric or nervous make-up often present in all ages, are apt to be exacerbated during the menstrual period, or during times of adolescent ovarian insufficiency, and especially in the menopause. On other occasions they appear for the first time in the critical age in women previously free from them. The phenomenon is well explained by the hypertonia of the visceral innervation or the influence of the hormones principally of the thyroid which directly excite the vegetative nervous system. Women affected with the spasm may present it constantly or at intervals. *In one of my cases it coincided with the days she should have menstruated.*

CASE 76.—Woman of forty-nine years. Always very strong. Hysteric attacks in puberty. During the period of ovarian activity she was very nervous, but had no other particular complaint. Menses regular; multipara. At forty-six the menopause began with excessive menstrual bleeding, regular for a long time. Marked suffocation; loss of weight; staring eyes; tachycardia; vasomotor instability and pains in the head and legs. Suddenly she began to feel some difficulty in swallowing. Seven months later *the menses skipped for the first time, coinciding with an exacerbation of the circulatory and nervous systems, and with severe spasms which prevented her swallowing any kind of food, solid or liquid.* This condition disappeared in the following days but was repeated in the subsequent months. Ovarian therapy and other prescribed remedies alleviated her general symptoms a great deal and also, although in less degree, the spasm. At present all the other climacteric symptoms have definitely ceased and she has days free from the spasm. Two years later it still persists and x-ray examination shows a slight esophageal dilatation evidently the result of its persistence.

The following case is also very typical, occurring in a climacteric woman with hypothyroid reaction:

CASE 77.—C. C. Forty-four years old, very robust; strong sexual character, with various hysteric phenomena in the course of her life, and hypothyroid symptoms with a tendency to obesity, edema of the eyelids and of the hands, very chilly, eyebrow

sign; menses regular; two children. She was left a widow at thirty-four and shortly thereafter began to have menstrual irregularities and various nervous and circulatory phenomena, nocturnal oppressions, palpitations and neuralgias, particularly at the time of her menstrual periods. She confessed the intensity of her sexual isolation which various considerations prevented her from breaking. Shortly after *she began to have from time to time pharyngeal spasms, which were not very marked*. At the fortieth year the climacteric phenomena appeared. She gained in weight in spite of all she could do. Her nervousness increased. The menses became very profuse and irregular. Hypothyroid manifestations were also marked and finally *the pharyngeal spasm became so intense* that after trying all treatments, nasal feeding became necessary for several days. In varying degree this condition lasted eight months becoming much better later on. Definite menopause occurred. She married again. Complete recovery.

In the diagnosis of these symptoms, *it should not be forgotten that the climacteric is the age of cancer and that neoplasms of the esophagus may begin with spasmodic symptoms*, all of which adds to the confusion. Doubtless, in the majority of cases, careful examination of the patient, her antecedents, and the course of the process, will clear up any doubt.

Spasm of the Cardia

A frequent form of these spasmodic phenomena is *spasm of the cardia*, which has been so well described by Madinaveitia.²⁷ Sometimes they are presented in women who have not suffered previously from this complaint. "Cramp in the cardia becomes evident by a pain, almost always sharp, which is felt in the upper part of the epigastrium and radiates to the chest. It is accompanied by a sensation of indefinable anguish. Almost always it lasts but a few moments, but when it is less strong it may last for some time. If food is eaten when the pain is at first felt it almost always ceases, for the painful contraction stops on the passage of food; that is to say, there is no permanent contraction like that of the esophagus which impedes the passage of food. Here there is cramp or painful contraction which does not

²⁷Madinaveitia: *Enfermedades del esofago y del estomago* Madrid, 1910.

inhibit the normal function. There are some individuals in whom it ceases instantly on the passage of food, but returns immediately." According to Madinaveitia sexual excesses are very frequently the cause of these cramps, corresponding to its frequency in the menopause. In one of my cases, the onset of the spasms coincided with mechanical irritation due to a partridge bone. But arising from this slight traumatism cramps developed with evident dependence on the menses in full climacteric involution; that is to say, the traumatism acted as the occasional cause on the heightened vegetative nervous system.

Nevertheless, let me state, that this symptom is often an index of an organic lesion, now local, now remote, especially cholelithiasis.

Climacteric Icterus

The *hepatic affections* in the climacteric crisis have been well studied, although to my way of thinking not correctly interpreted. Various writers, among them Kisch, Tilt and Frerisch²⁸ mention a *congested state of the liver* which occurs in the critical period. At times it may be discerned by palpation, but its sole clinical manifestation is apt to be a benign *jaundice*. This lasts from one day to several weeks generally without fever, if secondary processes in the stomach and intestines do not occur. In short the whole clinical picture is that of a mild form of so-called *catarrhal jaundice*. According to classic writers this hepatic congestion has a vicarious character.

In my opinion one should be very cautious in diagnosing such a condition as "climacteric icterus," as Blau²⁹ calls it, since—considering its rarity—it may be a simple coincidence of catarrhal jaundice which is common in the critical years. Moreover, one should not venture to give a benign prognosis lightly in the presence of a jaundice due to biliary retention after the fortieth year, for the reason that with the same symptom as the sole manifestation many hepatic cancers or cancers in the head of the pancreas begin. And these are frequent in this age.

²⁸Frerisch: Klinik der Leberkrankheiten, 1861.

²⁹Blau: Die Beziehungen der weiblichen Genitalorgane zur Leber. In Frankl-Hochwart: Die Erkrankungen des weiblichen Genitales in Beziehung zur inneren Medizin, Wien, 1912, i.

In some cases, nevertheless, the reality of climacteric icterus may be admitted if it coincides very precisely and repeatedly with periods of amenorrhea. Note the following case:

CASE 78.—S. de A. Forty-nine years old; always healthy, robust, without gastric, intestinal or hepatic antecedents. A short time before climacteric disturbances had begun; severe menstrual bleeding, mild circulatory symptoms, increase of weight and rheumatoid pains. *The first absence of menses which came without warning, coincided with the appearance of jaundice of catarrhal type, intense, without fever or subjective symptoms, and disappearing in six or eight days.* On palpation the liver felt slightly enlarged along the costal margin. This lasted ten or fifteen days. Menstruation returned the next two months after the use of ovarian extract. Amenorrhea the third month and a mild jaundice reappeared. In the following months the menopause was definitely established without further hepatic disturbances. This patient experienced a sexual upset, with veritable attacks of erotism.

Cholelithiasis. Pathogenesis of the Predisposing Action of the Menopause

Hepatic colics are presented with great frequency in the years which correspond to the climacteric. According to Urrutia³⁰ "in the man and in the nonpregnant woman biliary lithiasis ordinarily presents itself between the fortieth and sixtieth year." *In many cases lithiasic attacks appear for the first time in this epoch, coinciding very precisely with the critical period. In others, in whom this affection already exists, it is aggravated.* Women who complained of colic long years before and who appear definitely cured, have it again in the menopause. I have seen many cases of this kind.

At present we explain these attacks by taking into account the changes in abdominal circulation plethoric in origin, inherent in the climacteric and always very intense in the liver.

Moreover, let us recall (page 62) that in this age there may be

³⁰Urrutia: *Enfermedades del hígado*, in Hernando y Marañón; *Manual de Medicina interna*, 1916, i, III.

a hypercholesterinemia which has an influence on the appearance of hepatic calculi like that of pregnancy or that of typhoid fever.

Mikulicz's Disease. Its Relation to Genital Function

Let me note, in closing, *an affection related to genital insufficiency and therefore to the menopause—symmetrical infarction of the salivary and lacrymal glands, or Mikulicz's disease.* This curious development, not so rare as is believed, consists of infarct formation in the parotid, submaxillary, lingual and lacrymal glands on both sides, sometimes occurring without functional complaints and again with diminution of the salivary or lacrymal flow. The swelling does not involve all of the glands at once, but usually only certain of them in pairs—the submaxillary and lacrymal, for example, or only a single pair, like the parotids. In one case which I recently saw, only the lacrymal glands were swollen.

In the obscure pathogenesis of this syndrome there are only two definite points: (a) the coincidence of the infarcts with hemorrhagic lymphocytosis, sometimes a veritable leucemic state; and (b) *the coincidence of its appearance with different endocrine disturbances and particularly with genital insufficiency.* It was this last condition to which I was the first to call attention.³¹ Indeed, I have seen several patients in whom *this condition appeared at the time ovarian insufficiency was established, either early or at the regular age.* Recently I saw a very interesting case wherein the infarct was limited to the lacrymal glands, *yielding quickly and repeatedly in a perfectly demonstrable way to ovarian therapy.*

³¹Hernando and Marañón: *Enfermedades de las glándulas salivares*, in *Manual de Medicina interna*, vol. 1.

CHAPTER XX

RESPIRATORY SYMPTOMS

Epistaxis, Labored Dyspnea, Aggravation of Preexisting Diseases

Epistaxis has been mentioned with vicarious hemorrhages. *Labored dyspnea* originates in the abdominal fullness which is due to meteorism and the accumulation of fat. *Women with chronic respiratory lesions may suffer an aggravation of their condition during the congestive periods of the climacteric.* For example, tuberculous women may present hemoptysis (see the case cited on page 132, chronic bronchitis, or emphysema. Aside from these three types of respiratory disturbance, we shall study but one complaint in this chapter—asthma.

Asthma. Nervous Factor and Lesional Factor in Its Pathogenesis

Indeed, although asthma is a respiratory affection through its localization, in its pathogenesis it is a disturbance of the vegetative nervous system, like so many other conditions which we have studied. Taken together these might form a chapter under the title *Vegetative Disturbances of the Menopause*. But for the present it suits my purpose better to follow classic paths, especially when it is not certain that only a spasmodic element intervenes in the production of the asthmatic attack even in cases which appear to be purely nervous in type.

It seems probable that in persons with an absolutely sound respiratory apparatus, the nervous upset, however intense, could not produce a grave and lasting attack of asthma.

Hence many asthmatics are chronically ill from respiratory and circulatory diseases. Of course, one is apt to give the name asthma to simple attacks of sudden dyspnea, those due to a sudden disequilibrium of an already precarious respiratory apparatus. But I believe it is correct, in many cases, to include

under asthma attacks due to acute respiratory fatigue which such patients present, because the conditions under which the attacks appear and the objective examination of the patient during the attack gives proof of the existence of a bronchial spasm which helps produce the attack. In *asthma, properly speaking* and classically considered as a pure neurosis, the neurotic element, no doubt, greatly predominates over the lesional. But with careful consideration of the patient's antecedents and painstaking examination of her respiratory function between attacks, including an x-ray study of the thorax, it will almost always be found that there are latent lesions of various sorts, slight or even cicatricial, which fix the neurotic element upon the respiratory apparatus rather than upon any other organ or tract in the body. Walker,¹ among others, assumes that in all asthmatics there are lesions, more or less silent, of a tuberculous nature. I agree with him in admitting a lesional element in almost all asthmatics. But I believe that the lesion, perhaps in the majority of instances tuberculous may also be of another nature, adenopathic, bronchial, or representing disturbances of circulation through masked cardiac insufficiency. Close observation of a great number of these patients in the last few years has fully convinced me as to this point which I can only indicate here.

In those cases wherein the neurotic element is predominant the anatomic lesion, incapable by itself alone of producing symptoms, may have passed unperceived all during life. If the attacks are prolonged, the grave disturbance which they in turn produce on the respiratory organs may cause, according to my experience, these latent lesions to revive and develop vigorously. If this revival does not occur, when the nervous element disappears—that is, the attack—the whole complaint disappears clinically. Therefore, in practice, the study of this nervous element interests us principally, although we should not forget the other, the lesional, and thus avoid a grave diagnostic, prognostic, and therapeutic error.

¹Walker: Studies on the Cause and the Treatment of Bronchial Asthma, Jour. Am. Med. Assn., 1917, lxiix.

Action of the Pneumogastric Nerve

Of what does this neurotic or functional element constituting the essential part of the asthmatic attack consist? From the numerous theories² which have been advanced we may select these three well-known points which are definite: that is, *the influence of the hypertonia of the pneumogastric; the action of certain endocrine disturbances; the relation between the asthmatic attack and colloidoclastic attacks.*

The influence of the pneumogastric is well known and I need not dwell upon it. The bronchial terminal branches of the nerve are the ones through which is produced contraction of the bronchioles and the dyspneic attacks. This, then, is a true *vagotonic crisis*. Now since the equilibrium of the nervous system is broken, the factors which control this equilibrium must have intervened and we know the fundamental rôle which the internal secretions play in this direction. Thus, then, it cannot be denied that clinically and therapeutically an indubitable relation can be established between the two phenomena, vagotonia and endocrine instability. Here the most interesting of the endocrines are the suprarenals, the thyroid and the genitals. Let us examine them briefly.

Suprarenals and Asthma

In the pathogenesis of predisposition to asthmatic attacks a decisive intervention has been attributed to the suprarenals. The fundamental argument is the admirable alleviating action which adrenalin exerts on attacks of dyspnea—actually abortive at times. Every physician has proved this. And it might be supposed that an insufficient secretion of adrenalin and consequently a low tone in the sympathetic system would give rise to excitation of the pneumogastric, with a consequent predisposition to asthma, provided one accepts the concept, already commented upon on page 74, of the antagonism between the pneumogastric and the sympathetic function. But this hypothesis falls through lack of clinical support, for certainly states of suprarenal insufficiency such as Addison's disease should par-

²See Carrasco's summary; *Acerca de los nuevos conocimientos sobre la patogenia y el tratamiento del asma esencial*. Arch. de Med., Cirug. y Especial., Madrid, 1921, No 2.

ticularly predispose to asthma, a thing which never occurs. Hence we are forced to regard this antiasthmatic action of adrenalin as purely pharmacologic. In other words, it has a substitutive power, being effective symptomatically through its relaxing action on bronchial musculature and its blanching action on the bronchial mucosa which, being hyperemic during the attack, contributes to the obstruction of the lumen of the bronchial tubes.

Thyroid and Asthma

The intervention of the thyroid in asthma has been studied by Levi and Rothschild, Arrighi and others.³ These writers dwell on the frequency with which asthma appears in persons who present the symptomatology of *thyroid instability*, a condition which, as I have already said, coincides with the arthritic symptomatology, so frequent in asthmatics. Recently Bertolotti⁴ has described several cases of asthma in hyperthyroid subjects. He notes the accentuation of the symptoms during the attack and the beneficial effect of antithyroid serum. Therefore he attributes to hyperthyroidism an important rôle in the pathogenesis of predisposition and of asthmatic attacks. I have not confirmed these data in my cases of hyperthyroidism, but I wish to set them down here.

Gonads and Asthma

But the endocrine factor which we may relate to asthma with greater security is genital insufficiency. L. Levi⁵ has studied cases of true asthma in ovarian insufficiency, but to my way of thinking, he has not given this point its real importance for pathologists. No doubt the internal secretion of the ovary regulates the tone of the pneumogastric and the lack of that secretion, consequently, causes an increase of the tone. This is important, at the outbreak of the asthmatic attack. Perhaps along with this direct action of the ovary, the thyroid reaction which accompanies its insufficiency also contributes to the same end.

³See the literature on this question in Carrasco; *Op. cit.*, note (2), page 300, and *Dos casos de asma endocrino*. Archivos de Endocrinología y Nutrición, Madrid, July, 1924.

⁴Bertolotti: *Patogenesi é cura dell asma*, Acad. de Med. de Padua, 1916.

⁵Leopold Levi: *Pathogenie de l'asthme thyroïdien et ovarien*, Arch. gen. de Med., 1912.

The clinical fact is that a large proportion of cases of asthma appear at the climacteric, as various writers indicate without, however, giving any significance to this coincidence. Of 28 cases which I saw lately, ten were in menopausal women who until then had not suffered from this disease. Six were men and of these five were from forty to fifty years old. One was thirty-five, but with genital insufficiency. Therefore, in seventeen there was an evident relation between the asthmatic phenomenon and genital involution. Only in the remaining eleven cases could no relation be established between the asthmatic attack and genital function. It should be noted that of these seventeen cases several were patients with previous respiratory disturbances but they had never had asthma. As I have said before, these conditions have the same pathogenetic value as in cases of so-called "ideopathic" asthma, that is, free from evident lesions of the respiratory tract.

It is curious that but two of the studies on the critical age which I have consulted mention this interesting fact of the frequency of asthma in the climacteric. Fishberg has reported cases of asthma occurring during the natural or surgical menopause, establishing a relation between the generative function and the asthmatic phenomenon,⁶ and Recasens⁷ describes a case which demonstrates my hypothesis. His report is as follows:

"For three years, a patient had attacks of asthma of such severity that I feared for her life. These occurred after castration and as a consequence of it. Now after eleven years when the organism has become accustomed to the lack of the internal secretion of the ovary she has no attacks, which makes me think that the asthma she once had, immediately following castration, might have been of glandular origin."

Here is one of my own cases which is very striking:

CASE 79.—V. de N. Forty-six years old; always very strong; menses regular. Shortly after being married she contracted a gonorrheal infection with severe, painful metritic and perimetritic complications which required total extirpation of the internal genitalia at thirty-two. Shortly thereafter her husband died. A syndrome of ovarian insufficiency developed, not very

⁶Fishberg: Treatment of Certain Forms of Asthma with Ovarian Extract and Corpus Luteum, Med. and Surg., St. Louis, 1918, vol. II.

⁷Recasens: Op. cit., note (1), page 101.

marked, to which she paid little attention. *But some years later when she was forty-two, at which time she should have had her natural menopause, an intense climacteric symptomatology developed with persistent increase of weight, hypertension, severe suffocation, and great nervousness with the addition of attacks of typical asthma.* After various treatments these yielded to injections of corpus luteum extract. She had suffered much in her youth from catarrh but now presented no pathologic phenomena on the part of the respiratory apparatus.

Here are some typical cases occurring in the natural menopause:

CASE 80.—S. de R. Forty years old, always fat, scanty menses, sterile, that is to say with usual ovarian insufficiency. After the thirty-eighth year she had various hypothyroid disturbances and Quincke's angioneurotic edema. At her fortieth year she had a *typical attack of asthma* which came on suddenly and for the first time *during the days she should have menstruated.* Hence the attack had a frankly vicarious character. Upon energetic ovarian and thyroid therapy the menses reappeared later and the asthma did not recur even when amenorrhea finally became established.

CASE 81.—M. de E. Forty-one years old. Frequent attacks of "pneumonia and catarrh" in her youth. Menses always scanty. Sterile. At the fortieth year she had a *typical asthmatic attack.* She assured me there had been no change in menstruation and she presented no climacteric symptom except a moderate but persistent increase in weight. But in the following *months the menses failed to appear and the asthma recurred.* This lasted for several months. Condition very resistant to opotherapy and asthmatic remedies. Examination of the respiratory tract was negative.

CASE 82.—Ph. B. Forty-nine years old. Married; multipara; always well. *Climacteric at the forty-seventh year; with great suffocations and asthma which at the onset coincided with absence of menstruation* and continued from then on. In her youth she had had "much catarrh." Pulmonary examination, between attacks, was negative. Two years later she became diabetic and the asthma completely disappeared.

CASE 83.—D. G. Forty-five years old. Married, multipara, without interesting antecedents. Respiratory apparatus, always sound. At forty-three and a half years *the periods began to be irregular and an attack of asthma coincided with each disturbance*. She also complained of severe suffocation and increase in weight. Ovarian extract as the basis of treatment made her feel better. Two years later I saw her again at which time she was well.

The two following cases demonstrate very well my hypothesis. Both women had ovarian insufficiency and premature climacteric.

CASE 84.—S. S. Forty-four years old. Menses always very scanty. Sterile, fat, apathetic. *Menopause at the thirty-ninth year and since then great increase in weight and typical asthma*. Blood pressure 15-8. Thoracic x-ray examination, normal.

CASE 85.—J. G. Thirty-eight years old. Menses always normal but scanty; sterile and an associated tendency to put on weight. *For two years the skipping periods had been accompanied by asthma* which lasted two or three days with severe subjective distress; very noisy inspiratory rhoncus; tachycardia, hyperchlorhydria, polyuria and slight glycosuria not above 2 gm. per 1000. Treatment by rest, fresh air, gomenol-camphor and ovarian extract brought much improvement.

In closing, although it does not refer to the menopause, but because of its demonstrative value in affirming the relation of asthma to genital insufficiency, let me introduce the report of a case I published some time ago and which I have cited several times since.

CASE 86.—A youth of nineteen years with catarrhal antecedents; robust appearance; *attacks of dyspnea* which precluded any movement suddenly seized him. The most careful clinical and x-ray examination revealed not the slightest lesion of the respiratory organs. But one of the distinguished specialists who saw him noted *the imperfect development of the genitalia*. When I saw him I was convinced that he presented a case of spontaneous genital insufficiency with all the local symptomatology and general morphology of the eunuch and therefore attributed to this condition his attacks of fatigue. Therapeutic treatment completely confirmed my conjecture, for when he was subjected to

ovarian therapy the asthma quickly disappeared. On suspending treatment the respiratory attacks reappeared, to disappear again on the resumption of the remedy. This counterproof was repeated at two subsequent times. At the end of a year of sustained pluri-glandular therapy the retarded genitals had greatly increased in size and the respiratory symptoms had definitely disappeared. I should explain that I employ ovarian extract even when treating men because I believe that the genital hormones which act on the nervous system are not sexually specific, that is to say, they are common to both sexes. Clinical experience proves this brilliantly.

It would be desirable for physicians to try opotherapy in a complaint like asthma which is interesting both because of its frequency and its usual desperate resistance to treatment. The efficacy of ovarian extract in these cases which are related to genital insufficiency appear to me to be indubitable. Fishberg,⁸ who has employed indiscriminately extract of the whole gland and of the corpus luteum alone, expresses the same opinion.

Colloidoclasia and Asthma

In the last few years asthmatic attacks have been added to the group of symptoms produced by disturbances of hypersensibility or anaphylaxis. Or, as Widal and his adherents have said, disturbances of *colloidoclasia*. The experimental, clinical, and even therapeutic facts which show the anaphylactic mechanism of the asthmatic attack are really so numerous that there can be no doubt as to the relation existing between both phenomena. Widal, Abrami and Gennes recently attempted to reconcile this relation with the undoubted evidence just enumerated connected with the intervention of the endocrine factors in asthma. Their admirable article is widely known and has been much discussed.⁹ They hold that there is a "colloidoclastic diathesis"; that is to say, a constitutional state of colloidal instability which is propitious for the unloosing of the colloidoclastic phenomena such as urticaria and asthma. This "colloidoclastic diathesis" in

⁸Fishberg: Op. cit., note (6), page 302.

⁹Widal, Abrami and Gennes: Coloidoclasie et glandes endocrines. Presse Medicale, 1922, No. 36. See also my article Estado coloidal y glandulas de secreción interna. Medicina Ibero, June, 1922.

many cases may be linked with an imbalance on the part of the glands of internal secretion. They give an example of a patient with asthma in whom the attacks were provoked through an evident colloidoclastic mechanism—breathing the odor of roses. But this case was peculiar in that the attacks began with the appearance of menstruation at the fourteenth year, they were suspended during pregnancy, but reappeared afterward and stopped definitely at the menopause. Thus, contrary to the cases mentioned earlier, ovarian function in this woman produced the tendency to asthma. After the climacteric a myxedematous state developed whereupon the asthma reappeared. Both conditions, myxedema and asthma, were cured by thyroid therapy. This case which has been studied and reported in very great detail teaches us that the endocrine disturbance, ovarian and thyroid, *predisposed* to the attack and that the attack was brought on by means of colloidoclastic shock, in this instance the odor of roses.

Summary.—Let us sum up all this data. The colloidoclastic shock induced through a hypersensibility to some particular albumin or perfume, brings out as one of the typical clinical effects, the vagosympathetic disequilibrium located in the respiratory tract, which we call asthma. Certain endocrine disturbances (thyroid, genital, suprarenal, etc.) *predispose* to this phenomenon sometimes, as Widal says, through their direct action on the vagosympathetic equilibrium, or again through an excess, a defect or a qualitative change in the hormones, and this acts directly on the colloidoclastic equilibrium.

Mild Asthma. The Sigh Sign

All in all, the asthmatic attack, properly speaking, is a serious manifestation and one relatively rare. *Much more frequent are other less marked conditions which, to my understanding, are produced by the identical pathogenic factors causing asthma. I refer here to those short periods of respiratory anguish of which many climacteric women complain,* as do hyperthyroid women and women suffering from other diseases which affect the vegetative-nervous system. The attacks occur spontaneously or are the result of physical excitement brought on by exercise or they are psychic, due to emotion. Sometimes the attacks are nothing more than a

sensation of momentary difficulty in completing respiration, which obliges the patient to give a deep sigh, singly or repeatedly, after which she is comfortable. These attacks represent probably mild and transitory states of bronchial contraction and differ from true asthmatic attacks by the slighter intensity of the nerve stimulus. Perhaps in these, as we assume to be the case in true asthma, the respiratory apparatus is absolutely sound.

The fact is that this "sighing sign," so frequent in many nervous women, especially during menstruation, is present in a great many menopausal women.

CHAPTER XXI

URINARY SYMPTOMS

Outline

- (a) { Cystitis
Vesical calculi
Urethral prolapse
Cystalgia
- (b) { Hematuria
Polyuria
Renal lithiasis
Ectopic kidney
- (c) Uremia and menopause

Climacteric Cystitis

The urinary symptomatology of the menopause is not extensive. *The manifestation that I have observed most frequently is menopausal cystitis*, also mentioned by Kolischer¹ and Kermauner.² The symptoms are generally mild, often nothing more than frequency of micturation, with a sensation of tenesmus not very marked. It occurs in women who have previously been healthy or oftener in women who have had inflammation of the urinary bladder, as, for example, in pregnancy and the puerperium.

Cystoscopic examination shows (Kermauner) engorgement of the vesical mucosa at first. Later if the mucous membrane has been intensely and repeatedly affected, changes similar to those found in the senile bladder appear. The bladder takes on a pale and cicatrical aspect and shows scanty vascularization. The musculature of the wall is infiltrated with fat and its elasticity is decreased. Examination of the urine shows many epithelial cells, without pus (Kolischer).

L. Levi³ recently stressed the frequency with which *vesical*

¹Kolischer: *Erkrankungen der weiblichen Harnröhre und Blase*, Wien, 1898.

²Kermauner: *Beziehungen zwischen dem Harnapparat und den weiblichen Geschlechtsorganen*, in Frankl-Hochwart's book, cited note (19), page 102.

³Leopold-Levi: Private communication, Paris, 1918.

congestion is found in the menopause. Occurring in areas, these congested spots are interpreted as linked to the thyroid instability proper to the climacteric, and are present not only in the bladder, but in many other organs of the body, as the liver and appendix. Levi has carefully studied this congestion bringing to the task that clinical understanding which characterizes all of his endocrinologic work. Thyroid therapy in small doses is highly useful in these cases.

Here I make the same observation which I have so often emphasized in the course of this clinical study. That is, that the appearance of a cystitis in the climacteric may be a casual development or an aggravation arising from circulatory and nervous erethrism of a lesion latent until this time. This same neuro-circulatory erethrism, or "plethoric dyscrasia" as Aschner⁴ insists on calling it, may also give rise, alone or in combination with mild urinary symptoms, to a cystitis which merits the name climacteric. The mild urinary symptoms may represent marked eliminations of uric acid or minor infections of the mucosa. Here is such a case.

CASE 87.—S. E. Forty-seven years old. Multipara. No genito-urinary infections. For two months the menses were late and scanty. *The third month they failed to appear and a severe cystitis occurred.* This resisted all treatment for forty days. Cystoscopy; diffuse cystitis without swelling. Urinalysis, enormous elimination of uric acid, mucin, typical sediment, etc. Arterial tension 19-8. Opotherapeutic treatment by ovarian extract. In ten days *the menses reappeared and the cystitis disappeared* not to return. Now, two years later, complete menopause and a normal bladder.

Vesical Calculi

The dyscrasic changes which we have studied in this age favor the formation of *vesical calculi* with their proper symptomatology. For this reason I shall not describe it, also because it is really only very indirectly related to the climacteric.

⁴Aschner: Op. cit., note (31), page 255.

Prolapse of the Urethral Mucosa

Prolapse of the urethral mucosa, incomplete or complete, which Kermauner describes and which may be very painful, is an affection more proper to the atrophic states of old age than to the congestive period of the climacteric.

Cystalgia. Dysuria

Bardet⁵ particularly has studied the *cystalgia of the menopause*. In my opinion this is almost always consequent to frank lesions such as inflammations, calculi or ptosis. According to Vinay⁶ it may appear as does any neuralgia, that is, without the least symptom to suggest a vesical lesion responsible for the pain. The pains are apt to coincide with the beginning of micturition, lessening during its course. At times it coincides with incomplete retention.

Hematuria

Various writers have mentioned *hematuria* as occurring in the critical age. I shall make the same reservations here that I made in reference to other vicarious hemorrhages; that is, there is a possibility of hemorrhage being due to an organic lesion hidden until this time (page 130), but it can be produced through the climacteric plethora. This occurred in the following case.

CASE 88.—S. A. Forty-eight years old. Always well; without urinary antecedents; multipara. In the past year the menses failed for the first time. Copious hematuria, without pain or consequences, coincided with this suppression. Suffocation, great nervousness, hypertension (20-8). All this was repeated more severely in the following months. Cystoscopic examination normal. The symptoms did not recur.

Polyuria

Barbaud and Rouillard⁷ say that marked *polyuria* is observed in some women. I have already referred to this phenomenon in describing diabetes insipidus (page 68).

⁵Bardet: Traitement de la cystalgie de la ménopause. Bull. de Therapeutique, 1903.

⁶Vinay: Op. cit., note (12), page 19.

⁷Barbaud and Rouillard: Op. cit., not (18b), page 108.

Renal Lithiasis

Renal lithiasis, very frequent in the critical age has only one very indirect, very remote relation to it. The circulatory plethora no doubt has an influence upon the appearance of acute attacks in lithiasic states which have been latent up to this time. I mention it principally for the diagnostic interest which it may have in lithiasic troubles with various complaints of genital origin such as acute urethritis, uterine colic or salpingo-oöphoritis (Vinay).

Ectopic Kidney

Different writers mention aggravation of the phenomena dependent on *extopic kidney* in the menopausal period due to congestion of the organ. It can be palpated by vaginal examination. At present surgeons and specialists give much less attention than formerly to ectopic kidney in abdominal surgery. But the symptomatology is actually aggravated at times in the critical age.

Influence of the Menopause on Renal Diseases. Uremia and Menopause

In my opinion the most interesting topic for the physician in this chapter is *the influence which the menopause undoubtedly exerts on chronic diseases of the kidney*. I have observed an exacerbation of the symptoms arising from chronic nephritis in its various types when it occurs in women during this period of life. Le Gendre^s—I found no other mention of it in the literature—noted symptoms due to menopausal changes in renal function and attributed them to the congestion in the organ which lessens the quantity of urine excreted and thus produces a state of autointoxication. This, in its turn, further numbs the eliminating capacity of the kidney.

To the congestive and to the toxic element might be added the relation which undoubtedly exists between the climacteric and arterial hypertension. While this relation is debatable (see Chapter IV and XII) its reality is indisputable.

The fact is that, for all these reasons, the climacteric crisis can

^sLe Gendre: *La menopause et le rein*, Soc. Med. des Hop, 1897.

cause a pathologic deficiency in a kidney which has been in unstable equilibrium, but which has been apparently normal. Or it may aggravate any existing symptoms of renal insufficiency. Here are two illustrative cases.

CASE 89.—S. de B. Without important pathologic antecedents. Her first and only pregnancy terminated in an abortion which was badly attended. Immediately thereafter she suffered a uterine and later a pelvic cellulitis, with many months of septicemia. The attack terminated through spontaneous escape of pus. Suppuration continued for several months more. In the latter part of this period she presented some albuminuria. No other data available as to the urinary state. She had some flatulence.

She recovered from all this and was well for several years, although "always delicate." Probably a renal lesion was initiated during the long septicemia and prolonged suppuration, but it evidently developed silently, without giving definite manifestations which were noted during the patient's troubled life. At thirty-two the periods began to be irregular. Marked hypertension (18-9) appeared with frequent palpitation and slight glycosuria. Repeated urinalysis showed a low specific gravity and very deficient elimination, especially of nitrogen, but no albumin; normal sediment. *The first amenorrhea, at forty-three, coincided with an attack of dyspnea.* Slight pulmonary edema in the bases; hypertension; diminution in the total quantity of urine eliminated in twenty-four hours. Ambard's coefficient confirmed the intense renal retention and gave a grave prognosis. On an antiuremic diet associated with ovarian extract the attack passed. *Dyspnea recurred with pulmonary edema in the following month, during the menstrual period and with a similar course.* When the menses failed to appear for the third time, dyspnea was presented again with greater pulmonary edema and dry pleurisy sounds. Because of marked accentuation of the symptoms, another urinalysis was made. I lost sight of the patient. She died shortly after of uremia.

CASE 90.—M. T. P. Forty-eight years old. Infantile morphology and mentality; married; never pregnant; menses always

scanty and amenorrhea rather frequent. Among her antecedents, carefully inquired into *a posteriori*, there appeared scarletina, occurring in childhood, during the course of which she was "somewhat bloated." But other than this she had never presented any evidence of renal disease. Hereditary syphilis probable but not confirmed. As in the former case she had led a very retired life, uneventful, entirely compatible with her modest circumstances. Severe circulatory phenomena accompanied the menopause, hypertension and slight hyposystolic pressure. Various digestive disturbances occurred in a few months. These were thought to be indigestion. After one such attack *she suddenly sank into a frankly uremic coma*. Blood analysis confirmed this. *She died in a few days*. This no doubt was a case of latent nephritis which the climacteric crisis brought into relief.

I could give many other such cases although they are not so typical as these.

CHAPTER XXII

CUTANEOUS AND PILARY SYMPTOMS

Outline

- (a) { Eczema
Acne rosacea
- (b) Erysipelas, furunculosis
- (c) { Herpes Zoster
Hyperhydrosis
Erythema
- (d) Transient circumscribed edema (Quincke)
- (e) Pruritus
- (f) Melanoderma
- (g) { Hypertrichosis
Canities
Baldness

Eczema. Its Relation to Endocrine Pathogenesis

The skin suffers various affections on account of the menopause. The most frequent is *eczema*. In those women who have had it before, eczema reappears when they reach this age. It is exacerbated in those who have it at the time of the menopause. In many it makes its first appearance then. Its course is usually rather slow, a year according to Kisch.¹ This *climacteric eczema* is clinically like all eczemas. It is localized preferably on the face, head, fingers, legs and less often in other sites. Often it does not leave the patient until the climacteric period passes. It appears preferably in women of hypothyroid reaction. Ovarian therapy, and in these cases with hypothyroid base, thyroid extract has proved efficacious in my cases. Sometimes the results were excellent. This should incline us to this treatment in these cases especially as the complaint is so resistant to other remedies. It

¹Kisch: Op. cit., note (13), page 19.

is many years since Saalfeld² proclaimed ovarian substance as the treatment in these eczemas of mature women. Recently Bauer,³ Carreras,⁴ and others, have emphasized the coincidence existing between eczema and the climacteric, and the good effects of opotherapy.⁵

In my judgment, this relation, revealed in the clinic as existing between the menopause and eczematous processes, is an indirect pathogenic one. The various factors predisposing to eczema are all present in the critical age. Dermatologists offer autointoxications, nervous states and arthritis as predisposing elements. Moreover the humoral factor, which undoubtedly has a fundamental part in the pathogenesis of eczema, has not been well studied. I believe that more light will come from a consideration of the part played by the internal secretions. Thus hypothyroidism, although comparatively infrequent in the climacteric, is a condition propitious to eczema. I have demonstrated this in several cases as yet unpublished.

Acne Rosacea and the Climacteric

While rarely found in youth *acne rosacea* is very frequent from the fortieth to the fiftieth year. It occurs almost always in women. It appears in the form of symmetric hyperemic blotches, generally on the face, involving especially the nose and cheeks. On the red base of the congestion papules appear. These are red and small and become vesiculated in two or three days and covered with a small crust.

All writers mention the coincidence of this affection during the critical years. Sometimes they connect it specifically with changes in the genital tract. Among its symptoms they mention

²Saalfeld: Beitrag zur oöphorinbehandlung, Berlin, klin. Wchnschr., 1889.

³Bauer: Dermatoses und Klimakterium, Ztschr. f. Gynäk., 1923.

⁴Carreras: La opoterapia en sifillografia y dermatologia.—Rev. Sudamericana de Endocrinologia, etc., August, 1923.

⁵The recent literature relating to dermatoses and the internal secretions is most abundant. Among other recent summaries may be consulted: (a) Pulay: Die aus dem Einfluss der endokrinen Drüsen ergehenden therapeutischen Gesichtspunkte bei Erkrankungen der Haut. Therapeutische Halbmonatshefte, 1920.

(b) MacEwen: Relation Between the Internal Secretions and the Diseases of the Skin, Jour. Cutan. Dis., January, 1916.

(c) Pende: Op. cit., note (17), page 19.

(d) Covisa y Bejarano: Dermatologia y Endocrinologia, Ponencia al Congreso de Sevilla, October, 1924.

the frequency of *suffocation*, a phenomenon which is clearly climacteric. Thus it is very probable that besides the digestive and humoral factors which collaborate in its pathogenesis, an endocrine factor also intervenes, a relation which Vinay has pointed out.⁶ Caralt⁷ has recently studied this question and definitely declares that there is a hypogenital intervention in the pathogenesis of *acne rosacea*.

Erysipelas and Climacteric Furunculosis

The humoral changes linked to the sexual endocrine crisis have a marked influence on the defense processes of the organism against minor infections. This is the period for so-called *catamenial erysipelas* or for exacerbation of *furunculosis* during the menstrual days. The infectious agent, a streptococcus in the first case and a staphylococcus in the second, leads a precarious existence in the skin, dominated by the humoral defenses, consequently the clinical symptoms are slight or wholly absent. The humoral changes inherent in menstruation lessen these defenses and permit the germ to develop with greater virulence giving rise to the erysipelatous areas or to the deterioration of furunculosis. The intimate mechanism of this phenomenon is not yet known to us. But because the circulating lipoids bear so close a relation to the internal secretions, principally the genital and suprarenal, and because they play so important a rôle in the defence processes, it may be assumed that the changes in these lipoids have an influence on the reactivation of local infections occurring during the days of menstruation.⁸ If the menstrual flow is scanty or skips entirely, these cutaneous symptoms develop with a greater intensity. It would appear that absence of the menstrual discharge causes these humoral disturbances to become more marked thus favoring infection. The coincident congestive state aggravates the situation even more.

The same explanation covers cases of *menopausal erysipelas*, that is, chronic erysipelas which has reappeared often through-

⁶Vinay: Op. cit., note (12), page 19.

⁷Caralt: *Acné rosaceo y queratitis*, Archivos de Oftalmología hispanoamericanos, 1913.

⁸On this point see the interesting thesis by my colaborator Novillo: *Erisipela insuficiencia ovarica*, Arch. de Med., Cirug. y Especialidades, 1923.

out life and now returns with increased vigor and persists. It may return either in a permanent form or with periodic eruptions coincident with the days in which the menstrual flow should have appeared. All writers mention cases of this kind and I have seen several. In regard to *furunculosis*, it, too, is aggravated with relative frequency during the menopause in those women who have already suffered from it. Or it may make its appearance now for the first time. (Krieger, cited by Kisch.)

Herpes Zoster, Hyperhydrosis, Erythema

Many other dermatoses have been described in the critical age, but they cannot be interpreted except as mere coincidences without pathogenic relation to it. I shall mention only *herpes zoster*. I have seen this lesion in a considerable number of women as well as men during this age, but yet have been unable to fix upon its connection with the crisis.

I have already spoken of the *hyperhydrosis* from which some women suffer. It occurs chiefly when they have *suffocations* characteristic of this stage of life. A violent sweat bathes them, either localized or generalized. *I wish to call particular attention to the interesting observation that this profuse sweating may be observed in women who have never had such attacks before.*

Especially in women with deficient circulation and in the obese excessive perspiration predisposes to the formation of *erythemas*. Sometimes these are extensive, spreading over certain regions of the trunk, and appearing in areas as if stained red. They are frequently pruriginous and much later may acquire eczematous characteristics.

Transient Circumscribed Edema or Quincke's Disease⁹

Up to a short time ago this disease was studied in connection with the *localized adiposes* and *Meige's trophedema*. Although taking into account the clinical resemblances which link them, I cannot sanction this grouping. Clinically Quincke's edema is dif-

⁹Along with Castellino and Pende (op. cit., note (1), page 73), I believe that the name *angioneurotic edema* which has been given to this disease (Quincke's) should be abandoned. This name implies a pathogenetic concept which is probably inexact. The best name for this process is, in my opinion, *transient circumscribed edema*. This phrase correctly expresses the characteristics of the condition without presuming to express its mechanism in any way.

ferent from adiposes and trophedema in that it is always *transient* while the others are permanent. Pathogenetically, while adiposes and trophedema may be attributed to endocrino-vegetative disturbances, fugitive edema seems to be due to a colloidoclastic disturbance, an anaphylaxis, which brings it close to urticaria, already studied in Chapter XII. Because of these doubts, it seemed best to me to include Quinke's disease in the chapter on dermatology, since the skin is the preferred site for its manifestations.

Its *symptomatology* is well known. Local edemas, colorless or crimson, hard as contracted muscle appear at different points in the cutaneous tissue on the limbs, most frequently on the face, and sometimes also in the mucous membranes. These edemas do not pit on pressure. After some time they disappear without leaving a trace, though after frequent recurrences chronic swellings remain. These, indeed, resemble Meige's trophedema most strongly. The differentiation from urticaria is, in certain cases, very difficult to make as I have said.

The lesions themselves may appear without other manifestations or they may be accompanied by such subjective symptoms as tenseness or an indefinite sensation of hardness.

In my experience cases are rather frequent wherein all these signs and symptoms are presented in an attenuated form and may be interpreted as *mild forms of Quinke's disease*. It all comes down, then, to a subjective and objective sensation of elastic induration of the skin in certain regions of the body and of variable duration. Often these symptoms are so transient and mild that in spite of the patient's insistent complaints we come to doubt their reality, the more so because such patients are almost always neurotic. The exact condition may remain in doubt until, on some occasion, the swelling is actually seen by the physician.

Now although all writers point out that the most propitious age for the presentation of these edemas is before forty (Castellino and Pende say twenty to forty), *I would stress the frequency with which they appear in the climacteric*. Several writers, including Börner and Banke, have pointed out the coincidence of the edematous attacks with menstruation. Lewin saw a case with

an ovarian insufficiency in which the edema occurred when the menses failed to appear. Castellino and Pende state that there are "writers who have noted an aggravation of Quinke's edema during menstruation or the climacteric and have assigned a predisposing rôle to that condition."¹⁰ But, I repeat, my experience is definite regarding the influence exerted by premature or physiologic ovarian insufficiency upon the appearance of the disease.

As has been said, the present tendency is to consider this edema as a phenomenon of hemoclastic origin.¹¹ Some observers like Turnetini,¹² have succeeded in provoking the edema through the ingestion of certain foods, even bread. But no doubt here, as in urticaria, a state of endocrino-vegetative disequilibrium has a powerful influence on the ease and intensity with which this hemoclastic reaction appears. Without much doubt, therefore, the climacteric crisis with its ovarian insufficiency, its other endocrine imbalance and its neuro-vegetative instability, fulfills these predisposing conditions very well.

Pruritus

In Chapter XIII I have referred to *pruritus* as a simple neurosis and as an indication of metabolic intoxication—chiefly as the expression of prediabetic states or as a consequence of local affections, especially vulval kraurosis. I now wish to make the point that, whatever its mechanism, general or local pruritus coincides at times with ovarian insufficiency. It may be relieved either by ovarian therapy alone (Torre Blanco¹³), or by pluriglandular therapy (Izondi and Haas¹⁴).

Climacteric Melanoderma; Its Pathogenesis

In a considerable number of cases onset of the climacteric is announced or it is accompanied by the appearance of dark pig-

¹⁰See the bibliography in Castellino and Pende: Op. cit., note (1), page 73.

¹¹See Phillips: Jour. Am. Med. Assn., 1922, lxxviii.

¹²Turnetini: Bull. et Mém. de la Soc. Med. des Hôp. de Paris, 1922, xvii.

¹³(a) Torre Blanco: Prurito vulvar e insuficiencia ovarica. Archivos de Med. cirug y Especialidades, July, 1924, No. 2.

(b) See also Sánchez Covisa (I): Patogenia y tratamiento general del prurito. Discurso inaugural de la Acad. Med. quirurg., 1922-23.

¹⁴Izondi and Haas: Essentiel Pruritus, München. med. Wehnschr., April, 1922.

mentations on the skin. These lesions take the form of patches appearing as a *general darkening* of the skin wherein are grouped together very tiny punctiform spots which detach from the base. *These are localized preferably on the temples, forehead, upper lip and less often other regions of the body.* Localization on the nipples and on the external genitalia is less frequent than in Addisonian pigmentations. Localization on the mucous surfaces, so typical of Addison's disease, is rare.¹⁵

This type of pigmentation is presented not only in the menopause, but even with greater frequency in other functional changes involving the genital tract. Occurring in pregnancy as "*liver spots*," the lesions are a typical manifestation. In ovarian cysts, uterine disease and various other genital lesions and also in the ovarian insufficiency of adolescence they constitute a very common symptom, one to which writers have not called much attention.

The pathogenesis of these pigmentations does not appear to me to be clear considering the data we possess at present on pathologic melanodermas. We know, for instance, that suprarenal insufficiency, through disturbance in the production of adrenalin and the cortical lipoids, causes dark areas on the skin typical of that disease. But I have already stated that the localization of genital pigmentations does not coincide exactly with that of suprarenal pigmentation. Moreover, the general symptoms which always accompany Addisonian melanoderma do not exist.

In these cases, therefore, without denying a collaboration on the part of the suprarenal organs in the production of the discoloration there are those who admit the probability of a frankly genital origin. Pende describes "pigmento-lipoid combinations," but these are not due exclusively to lipoids of the suprarenal cortex since they also exist in the genital glands. And the disturbance of either by a mechanism even less understood may cause climac-

¹⁵These peculiarities and the fact that they are not accompanied by hypotension, asthenia, hypoglycemia, and such developments proper to suprarenal insufficiency, differentiate very clearly the *pigmentations linked to ovarian upsets from those plainly Addisonian*. I do not agree with Sezary, who considers them all endocrine melanodermas. (Pathogenie et semiologie des melanodermies du type addisonien. Press. Med., 1921, p. 281.)

teric pigmentations. McEwen¹⁶ draws similar conclusions in studying these genital pigmentations.

Climacteric pigmentations are presented alone or linked with various general symptoms. On occasion they give rise to well-delimited syndromes, such as that I described under the term "bronzed virilism" (page 278), or the one just detailed.

Neuropigmentary Syndrome of Celibacy. Examples

Climacteric pigmentations are very frequently observed in celibate women, especially in those who remain unmarried contrary to their inclinations, in young widows, or in wives whose husbands are impotent or absent for long periods of time. In these the menopause may occur early or not, but it always develops with severe phenomena particularly when the patient is neurotic. Bloch¹⁷ has described this combination of pigmentation and a varying mental reaction in celibate women. I believe that, although somewhat exaggerated, his description is accurate in a great number of cases. Here are two interesting examples.

CASE 91.—C. M. Unmarried; without interesting antecedents. Of several fiancées she had married none, but for reasons usually not in accordance with her wishes. At thirty-nine she began to suffer the following complaints: (a) *digestive disturbances* and constipation; (b) *nervous symptoms*, severe asthenia, poor emotional control, melancholia, irritability, insomnia, and persecutory ideas; (c) manifestations of a *mild hyperthyroidal reaction*; loss of weight, tachycardia, palpitations and tremor of the hands; (d) *a diffuse melanoderma* formed of pigmented patches on the forehead, cheeks and other regions, making one think of *hepatic affection*; (e) *menstrual disturbances*; first severe metrorrhagia, then irregularities and amenorrhea. I treated her for one year with

¹⁶MacEwen: Op. cit., note (5b), page 315.

¹⁷Bloch: A New Syndrome, Med. Rec., 1916. I have not read the original article, but there is a long reference in Press. Med., 1917, No. 15, with ironic comment, perhaps unjust. It may well be that Bloch has not described a "new syndrome." But it is indubitable that his description corresponds to a clinical reality which generally escapes the physician's eye. Following the cases published in the first edition of this book, mention should be made of a case reported by Juarros: Un caso de síndrome de Bloch. Acad. Med. Quirurg. (Madrid) 1921-22. I have seen several more wherein I confirmed the frequency and the regularity of the syndrome. They will be published soon together with adequate discussion by my collaborator, E. Bonilla.

ovarian extract, antithyroid serum, belladonna, together with suitable dietary management. At the present time she has not yet passed through the critical period.

The coincidence of early menopause, sexual abstinence and pigmentation is very clear in this case which closely resembles those described by Bloch.

CASE 92.—H. de A. Valencian; without important antecedents; unmarried. Wholly devoted to religious practices. She had made her home life almost monastic. *Pigmentation* on the face began to appear at the fortieth year and was mottled by darker spots, especially on the forehead. Its appearance coincided with various *digestive disturbances* such as colic and painful biliary vomiting. A diagnosis of hepatic disease was made and she was sent to Cestona where she became worse. Great asthenia, *melancholy and loss of weight* developed, all of which were attributed to the liver. I demonstrated the soundness of the liver and regarded her cutaneous, nervous and digestive symptoms as being climacteric manifestations—indeed amenorrhea had been present two months. Ovarian and suprarenal extracts, diet and psychotherapy greatly relieved her of all her symptoms, including the pigmentations.

In this case I am not sure whether her unmarried state had been voluntary or whether she had ever been disturbed by sexual disappointments. When I knew her, her piety and religious trend seemed to remove all suspicion of sexual impulses. Her excessive mysticism is, no doubt, pathologic. Note also in this clinical history, the diagnostic error of "liver trouble" as a result of the pigmentation. In the previous case and in the one to be described next the same error occurred—a very common one among us. I have often seen at our baths, which bear a reputation for efficacy in hepatic diseases, patients with all the aspects of suffering from Addison's disease or genital disturbances.

CASE 93.—H. de S. (Santander.) Always very nervous. Intelligent; severely moral. She had had several unfortunate love affairs in her youth which resulted in her becoming preoccupied and caused her to repel further opportunities for marriage. At

the thirty-fifth year she began to suffer various nervous disturbances which became intense. At certain times these were frankly psychopathic, taking the form of persecutory delirium, melancholy and certain manias, all aggravated during menstruation. Vague digestive symptoms occurred a little later especially flatulence and aerophagia, and dark yellowish spots appeared on the forehead, cheeks and breast. These at first were transient but later became permanent and darkened. In this case too there was supposed to be an hepatic disturbance. Her symptoms continued for one year with various fluctuations. Loss of weight and tachycardia suggested hyperthyroidism. Menstrual periods began to skip at the thirty-sixth year and shortly after they ceased entirely. Her nervous disturbances were extraordinarily aggravated by the thought of approaching old age and the definite loss of sexual hope.

Disturbances of the Pilary System. Hypertrichosis, Canities, Baldness

In Chapter XVIII I took up the subject of *hypertrichosis*, its pathogenesis, its various grades and its symptomatologic significance. Another disturbance of the pilary system which must be considered is whitening of the hair. *Canities* is a symptom which is not climacteric but senile. Yet it is apt to begin early in the menopausal period because here, no doubt, it finds pathogenic conditions appropriate for its appearance. I have insisted strongly on the *relation of early gray hair to hyperthyroidism*. These women whose hair turns white prematurely are very frequently hyperthyroid. In almost all cases of hyperthyroidism a rapid increase in grayness is likely to be observed, the hair sometimes becoming completely white. Again it is not a frankly hyperthyroid condition but one of *thyroid instability* with hyperfunctional attacks. Hence the frequency of canities in hypothyroidism, an observation not new and one recently discussed by Lorland.¹⁸ We can only conjecture as to the nature of the mechanism which relates thyroid disturbances to the appearance of gray hair, but it is undoubted. Hence, because of its fre-

¹⁸Lorland: Haarausfall, Glatze, Haarergrauen. Leipzig, 1922.

quency, hyperthyroidism, or at least thyroid instability, may explain or help to explain climacteric canities.

It would appear that premature whitening should be a manifestation of premature senility and therefore of premature menopause. But not only is this not so, as I have observed in many cases, but *on the contrary premature whitening coincides with a prolonged conservation of the woman's physical, mental, and sentimental youth, and therefore with persistence of sexual activity with abundant menses and marked symptomatology, the hyperthyroid phenomena, therefore, predominating.*

I have also indicated *the frequency with which women with prematurely white hair present rheumatic manifestations in the menopause.* Lorland has called attention to this in his study of patients showing metabolic disturbance, it being especially marked in the diabetic Jews.

Regarding *baldness*, it may begin in the climacteric epoch, especially when there are hypothyroid or hyperthyroid symptoms. Lorland has studied this problem with his usual acuteness, detailing the relations discovered between the genital function and canities, baldness, and skin discoloration. These relations are so close that, for him, "the skin of each individual is in a certain way the projection of his genital function." In his opinion it is always the thyroid which is responsible for these changes in the pilary system, thanks to the close interdependence of this gland and the gonads.

CHAPTER XXIII

OCULAR AND AUDITORY SYMPTOMS

Ocular Hemorrhages and Inflammations

The "plethoric dyscrasia," the climacteric hypertension, on one side, and the endocrine changes which concur in the climacteric crisis, on the other, may have an influence on the appearance of latent ocular states. Or these may be aggravated if they already exist.

Poyales has carefully studied ocular symptomatology in diseases of the glands of internal secretion.¹ He describes two groups of symptoms as being very frequent in the menopause. In the first group come *subconjunctival* and *retinal hemorrhages*. The former are not serious. The second are more important since they affect visual acuity. In the second group we find *persistent inflammatory states of the internal membranes and of the optic nerve (iridocystitis, neuritis)*, "rebellious to all treatment and which, occasionally, seriously compromise the patient's vision."

González² also has observed, in menopausal women, *conjunctivitis iridocapsulitis* and *iridochoroiditis*. He emphasizes the favorable effects which in such cases he has obtained with opotherapy.

Glaucoma and Climacteric

Paltracca,³ González (op. cit.), and others point out the coincidence of the climacteric symptoms with glaucoma, a fact which I, from the point of view of a general practitioner, can confirm. Paltracca frankly assigns to glaucoma an etiology frequently endocrine, related to the hypertension due to the genital insufficiency of the climacteric. He advises opotherapeutic treatment, ovarian extract and testicular, as coadjuvant to the classic remedies.

¹Poyales: Las secreciones internas en oftalmología, Madrid, 1923.

²González: Conjunctivitis en la menopause: Medicina Ibero, 1922, No. 353.

³Paltracca: Etiologie dell glaucoma; Giornale di Oculistic, 1922, No. II.

Edema of the Eyelids

Poyales says he has "observed persistent *edemas of the eyelids* which may go so far as to give the patient a myxedematous aspect. These are resistant to treatment and investigation as to other etiologic causes is negative." I question, at least in some of these cases, whether this swelling may not be due to hair dye. In this, the age of cosmetic agents, I have seen some cases of persistent palpebral edema which have been treated as nephritis, cardiac trouble, and myxedema. Some of these finally consulted me and I have demonstrated the relation between the edema and the immoderate use of hair dye. Merely the discontinuance of the dye made unnecessary the array of remedies they had been using. But, let me add, sometimes one must wait patiently for the return to normal.

Cataract and Climacteric

The relation, at least chronologically of cataract with the critical age, is a fact of frequent observation. We must not forget that this is also the age propitious for diabetes and the prediabetic states. For this reason the practitioner will not fail to have urinalyses made in the presence of a suspicious obscurity in the lens. Tests also should be made for alimentary glycosuria, glycemia, and arterial tension to check up on an early stage of diabetes. González is inclined to believe that, apart from these cases, the endocrine disturbance of itself may favor cataract. This appears to be so in the following case:

CASE 94.—V. G. Forty-two years old. Always fat, with tendency to hypertrichosis, with scanty menses and sterile; that is, *with ovarian insufficiency. At the thirtieth year the menses stopped. Two months later, cataracts appeared. Glycemia, normal, 0.0097. Basal metabolism, normal, +9. Wassermann negative. Her mother was diabetic. Therefore, clinically a condition of youthful and inexplicable cataract coincided with premature genital cessation.*

Ear Noises and the Climacteric

The critical age frequently coincides with the beginning of the *ear noises* which occasionally render so unhappy the last years of

some persons. As is known, these buzzings are due almost always to a sclerotic state of the internal ear incident to the general sclerotic degeneration. The plethoric upsets of the climacteric are limited to bringing into relief the complaint latent up to that time. But again it *appears that the functional hypertension and the great circulatory erethism of this age may be sufficient to produce the phenomenon*, as Leighton⁴ says. I, too, have proved this in some cases wherein on the disappearance of hypertension the auditory distress also disappeared. In every way I subscribe to Leighton's statement that the sphygmomanometer is an indispensable instrument in all medical consultation, including that of specialists who seem furthest from this sector of pathology, as in oto-rhino-laryngology.

If the climacteric woman suffers hypothyroid symptoms, the edematous infiltrations of the auricular mucosa may often assist in causing the buzzings, as we have seen. In these cases the complaint disappears under thyroid treatment.

⁴Leighton: Organotherapy in Diseases of the Ear, Nose and Throat, Brit. Med. Jour., November, 1924, p. 1923.

CHAPTER XXIV

THE ARTIFICIAL OR SURGICAL MENOPAUSE

Fundamental Distinction Between Artificial and Physiologic Climacteric

At various times in the course of the preceding pages I have explained the fundamental fact which must serve as a basis for our clinical interpretation of surgical menopause in respect to the concept of the critical age which I have attempted to sustain in this book.

That basic fact is the following: *So-called surgical menopause is clinically the expression of total and sudden ovarian insufficiency, while the spontaneous climacteric is a complex, pluriglandular crisis, of which gradual ovarian insufficiency forms the nucleus surrounded by other diverse endocrine reactions.* This difference in pathogenic concept accounts for the differences which we observe clinically between the two states.

Dissociation of Ovarian Symptoms from Other Endocrine Symptoms in Castrated Young Women

As the endocrino-vegetative reaction, which characterizes the spontaneous climacteric, is conditioned by the anatomic and functional state possessed by these glands in maturity, which is wholly distinct from that which they have in youth, *castration will give rise to symptoms more like those of the spontaneous critical age as the operation is performed nearer the climacteric age, forty to forty-five years.*

I would call the attention of practitioners to this interesting phenomenon. In women with a rather stable endocrine equilibrium, who are castrated in youth, we frequently see *the symptomatic dissociation between the menopause and the climacteric* to which I have referred on page 35. In such cases we see first a series of manifestations most closely linked to ovarian insufficiency. This follows close after castration and then more or less com-

pletely disappears. On reaching the age in which spontaneous menopause should occur various disturbances appear, dependent on the endocrino-vegetative reaction although this is mild because of the inactivity of the original phenomenon, ovarian insufficiency. Of many such cases which I have collected in the last few years here are two very characteristic examples of this *dissociation*.

CASE 95.—A. de M. Very strong woman; always healthy; menses regular. Married six years; no children. Her sterility was attributed to various causes and she submitted to different methods of treatment in order to have children. During a manipulation of the uterus with this intent, infection and inflammation resulted so intense and stubborn that *extirpation of the uterus and ovaries was considered necessary*. She was then thirty-two. The operation relieved her of her local complaints and only produced, as general phenomena, *a considerable increase in weight, 56 to 68 kilograms in two years, and not very intense "suffocations."* Other than these and the menstrual cessation, she had no symptoms. But *at her fortieth year the suffocations were intensified and became more frequent. A sensation of circulatory fullness alarmed her greatly. At the same time various nervous disturbances appeared, neuralgias and psychic excitation, and flatulence.* In the following year her husband died and after this emotional period all her subjective complaints were extraordinarily accentuated. Hypertension averaged 18; massive appearance; thyroid hypertrophy; moderate tachycardia of 88; palpitation; very intense oculo-cardiac reflex (88-78); that is to say, *the usual manifestations of spontaneous climacteric crisis*. Ovarian therapy in very large doses relieved her complaints but have not entirely disappeared, though two years later she was much improved.

CASE 96.—S. de T. Always well; of asthenic constitution; scanty but regular periods. She married at twenty. No children. Shortly after her marriage a gonorrheal adnexal inflammatory process began which, two years later *required total castration*. Gynecologists told her that after the operation she would have severe suffocation and nervous disturbances but *she experi-*

enced no other distress than some mild and transitory suffocation, attacks of diarrhea corresponding to the time of her regular menstrual periods and considerable though not excessive increase in weight. All these symptoms lessened and she was well until her thirty-eighth year, when, coinciding with the distress and worry produced by her husband's condition of grave neurasthenia, she began to complain of severe suffocations. In association with these she showed extreme change in character which she herself noted, loss of emotional control ("I cry for everything," she said), very profound morning weakness, insomnia, accentuation of diarrhea especially under emotional stress, mild tachycardia (90), sensations of precordial oppression, moderate hypertension (average 18), slight hirsutism on the upper lip and cheeks—in short, a typical climacteric syndrome. I began opotherapeutic treatment but I do not know its results.

Thyroid, Suprarenal and Hypophyseal Factors in Surgical Menopause

Thus the glandular crisis which I described in the normal climacteric appears in surgical menopause with *lessening intensity* in proportion as the mutilation is earlier. In regard to *the type of these reactions* it is impossible to differentiate them from those of the spontaneous climacteric without becoming too didactic. I stress only the fact that the younger the woman the more likely are hypothyroid reactions to predominate over the hyperthyroid, as I explained on page 41.

[This difference between the surgical and the physiologic climacteric cannot be too strongly emphasized, and the author has made it clear according to our present knowledge of endocrine physiology. I offered an explanation of this based upon the theory of duration of association in my paper in 1916.—C. C.]

But this is not an absolute rule for we do see cases of *typical hyperthyroid reaction in women castrated in the midst of youth*. This happened in the following case:

CASE 97.—C. S. de R. From the first menstruation at fourteen the periods had been irregular and scanty. Asthenic type; nervous; periods of slight fever (37.5° to 38° C.) exaggerated during menstruation. The year she married severe ovarian pains coincided with menstruation, with increase of fever, and leucorrhea. In

the twenty-fifth year both ovaries were extirpated, one of which was found to be much atrophied. She was very well the first year following the operation. The fever and pains disappeared and she gained considerably in weight. Then a *typical hyperthyroid syndrome* developed. She lost weight rapidly and without cause; suffered severe suffocations; tremor of the hands; pulse of 100; sweating; severe nervous excitability. Normal arterial tension (15 Riva-Rocci). I do not know the results of the treatment, antithyroid serum, ovarian extract, diet and rest.

Of the hypophyseal reaction I can say nothing. Sometimes the obesity and dullness which follows castration somewhat recalls Fröhlich's syndrome. Again, on the contrary, acromegaly may follow ovarian extirpation. This occurred in the case referred to by Goldstein¹ and in the case of Fig. 16, use of which I owe to Dr. Pascual's kindness.

Aside from the age, whether the glands will react in one way or another certainly depends upon *the patient's endocrine constitution*. In Goldstein's case there was a frank hyperfunctional predisposition on the part of the hypophysis and an analogous observation could be made in other cases.

The Ovarian Factor

But if the complementary glandular reaction is, in general, much less marked in young castrated women, the symptomatology depending on the ovarian insufficiency, properly speaking, may be much more marked. While in the climacteric it is a matter of slow, progressive, and therefore more easily borne, extinction of the ovarian secretion, in castration the suppression is sudden and may surprise the gland in full functional activity. Fortunately, as regards these postoperative consequences, when ovarian extirpation is necessary the ovaries are almost always inflamed, cystic or otherwise, and consequently in a functionally deficient state. [Every gynecologist is well aware of this persistence of ovarian function in the face of systemic disease and in the face of ovarian inflammation, even suppurative, and of neoplastic change. Indeed this function yields sooner to systemic disease than to local.

¹Goldstein: Ein Fall von Akromegalie nach Kastration bei einer erwachsenen Frau, München. med. Wchnschr., 1913.

It is often surprising how well menstruation persists, and even pregnancy occurs, in the presence of ovarian abscess and neoplasm. For this reason the indications for bilateral oöphorectomy in young women is practically limited to extensive suppurations and proliferative neoplastic developments.—C. C.]

This softens the transition to absolute ablation. And to this circumstance we may add another which is very interesting, *the*



Fig. 16.—Acromegaly consequent to castration.



Fig. 17.—The same patient as in Fig. 16, at twenty-three.

possibility that the genital hormone remains active in the organism for some time after the glands are extirpated. This is inferred from some most interesting facts brought out by experiments on male frogs in which for some months after castration the genital reflex could be provoked. Explanation of this assumes that the nervous tissue is left impregnated with the internal genital secretion (erotization of the nervous system) and so long as this stored-up reserve is not exhausted, libido can continue. Steinach

succeeded in provoking libido in a castrated toad both with testicular extracts and with extracts from the nervous system from uncastrated males. But such extracts from castrated males did not have the same effect.²

Action of the Uterus and of Menstrual Retention

I have already explained in Chapter XII the studies of Graves, Ramirez, and others, on *the probable rôle which the uterus plays in the pathogenesis of the symptoms previously attributed solely to oöphorectomy*.

Aschner³ insists on the importance of the *retention of the menstrual blood*, which causes a certain state of autointoxication. According to him, the glandular reactions which accompany castration are means of defense against this intoxication. And the greater part of these symptoms which have been considered as due to ovarian insufficiency would really be toxic symptoms.

In regard to the intervention of the uterus, I repeat that my experience is against giving it an important part in climacteric symptomatology and surgical menopause, since *the typical phenomenon of this state, suffocation, is observed with greatest intensity in cases of castration by x-rays*. And in these the uterus presumably escapes and remains in a rather normal state. It is more likely that the absence of menstrual discharge, menstrual retention, exercises a toxic action, to counteract which it may be presumed that the organism has defense mechanisms. At any rate this does not prove Aschner's hypothesis.

[The fate of the uterus after ovarian ablation is one of decline by atrophy, regardless of the age of the patient. Where castration is effected by the x-ray, there may be some doubt as to this change, but the idea generally prevalent in the United States is that it is much the same as castration by radium, when, of course, the uterus is directly affected by the emanations. We find it difficult to think of the uterus as remaining unaffected after radiation by the roentgen ray sufficient to cause cessation of ovarian function, even temporarily.—C. C.]

²See Athias: Op. cit., note (2h), page 186, and Steinach: Op. cit., note (20), page 31.

³Aschner: Op. cit., note (31), page 255.

Medical Circumstances for Postoperative Prognosis

All these possibilities should certainly be taken into account by the gynecologist before deciding on castration. Fortunately, less and less are operators relying on a local lesion alone in deciding upon this course. The local lesion may, at times, compel the surgeon to work in a particular way, relegating to second place that phase of the problem which we may call medical. But in the majority of cases, the remote consequences of castration should be gravely comprehended. We may thus sum up the circumstances which the gynecologist should have in mind before deciding on intervention:

1. The proximity of the critical age (forty years) will render the secondary disturbances more turbulent but also briefer.

2. The greater the previous soundness of the ovary the greater will be the intensity of the endocrine disturbances.

3. Women with previous endocrino-vegetative imbalance, temperamental or pathologic (*hyperthyroidism, hypothyroidism, etc.*), will certainly experience much more turbulent reactions than women *with previous endocrine vegetative equilibrium.*

4. The patient's psychic condition will greatly influence the symptomatology of surgical menopause. By psychic conditions I refer to the woman's nervous and mental antecedents and the normal or abnormal state of the mental, emotional and sexual environment.

5. At any rate the aim of the operator should be *to conserve all that he can.* The internist's ideal is fulfilled when, despite mutilation, the uterus is conserved together with some portion of ovarian tissue. This is often possible in the chronic inflammatory processes which are the principal reason for surgical intervention.

[An extended argument upholding this attitude was offered in my paper* on the disposition of the uterus following salpingectomy where ovarian conservation is possible. The preservation of menstruation, that is, of uterine activity, is believed by many of us to have a definite value.—C. C.]

*Culbertson, Carey: The Disposition of the Uterus Following Salpingectomy Where It Is Desirable to Preserve Menstruation, *Am. Jour. Obst., and Gynec.*, 1921, ii, 497.

This diversity of factors, which are of so distinct and even opposite action, explains the qualitative and quantitative variety of the symptomatology of surgical menopause. It also explains why gynecologists are so little agreed in this respect. While Kisch⁴ and Schickele,⁵ for example, claim that as a rule surgical menopause has a symptomatology less grave than the normal, Vinay and, in general, the French writers, and Recasens⁶ affirm the contrary. On the other hand, while the majority of writers claim that *the symptoms of castration are more intense in proportion to the youth of the woman* (Prochownik, Richelot, and Routier, cited by Levy⁷), other observers think the contrary, that is, *that in women of mature age castration produces complaints as great or greater than in young women* (Canu,⁸ Muret,⁹ Jayle,¹⁰ Chrobak,¹¹ Mainger and Schmalfus, cited by Levy (op. cit.)). No general rule can be laid down to cover all of these points, since *the effects, influenced by the conditions which I have just explained, vary in each case.*

Cases without Symptoms

Because of these same conditions artificial menopause *may have no subjective clinical consequences.* There may be no true symptomatology just as sometimes occurs, but less often, in spontaneous menopauses. According to Maclaure's¹² statistics only 5 or 6 per cent of castrated women present complaints. This figure is evidently too small. Although my experience has no great value here, because the castrated women who consult the internist are just those who feel distress, my impression is, on the whole, that *at least two-thirds of those operated upon have disturbances of varying intensity.*

⁴Kisch: Op. cit., note (13), page 19.

⁵Schickele: Op. cit., note (14), page 19.

⁶Recasens: Op. cit., note (1), page 101.

⁷Levy: Op. cit., note (6), page 19.

⁸Canu: Resultats therapeutiques de la castration, Paris Thesis, 1896.

⁹Muret: De l'organotherapie par l'ovaire, Rev. méd. de la Suisse rom., 1896.

¹⁰Jayle: Opothérapie ovarienne contre les troubles consecutifs à la castration chez la femme, Press. Méd., 1896.

¹¹Chrobak: Ueber Einverleitung von Eierstockgewebe. Zentralbl. f. Gynäk., 1895.

¹²Maclaure: L'insuffisance ovarienne, Jour. des practic., 1904.

Chronology of the Operative Consequences

The symptoms begin at various periods after castration. According to Schickel  (op. cit.) they appear from the tenth or twelfth day up to months afterward. Levy (op. cit.) gives two to three weeks as the most frequent interval but cites cases in which symptoms appeared in four days.

In reality, it is difficult to give fixed rules on this point, since the date of the appearance of the symptoms, like their intensity and their duration, depends on all the conditions which I have enumerated before—the age of the patient, the state of her endocrine and nervous systems, and so forth. That is to say, their appearance depends on a combination of factors which are absolutely personal and distinct in every case.

Review of the Symptomatology in Castration. Genital Symptoms. Persistency of Menstruation

The symptomatology of castration is essentially similar to that of the physiologic critical age. But there are, nevertheless, certain peculiarities which make a rapid review of its principal symptoms useful.

The *genital symptoms* are limited to definite suppression of menstruation. Generally, during the first months or years which follow castration, the woman experiences some local and general distress during the days menstruation should have occurred, which reproduce more or less completely those which used to accompany the period. This phenomenon occurs especially in very nervous women which indicates the influence suggestion has in its genesis.

On rare occasions menstruation has persisted for some time after ovarian ablation. According to Pfister, cited by Pende,¹³ this occurred in 12 per cent of cases. This fact may be interpreted as a consequence of incomplete extirpation, some of the ovarian tissue remaining in situ, either through defective technic or through the existence of accessory ovarian tissue. We must admit this explanation even in those cases where an attempt has been made to exclude it, as in the case published by Palmer Findley.¹⁴

¹³Pende: Op. cit., note (17), page 19.

¹⁴Palmer Findley: Menstruation in the Absence of the Ovaries, New York Med. Jour., 1912. Ref. by Rebaudi in Pathologica, 1914.

Findley's report concerns the case of a woman who was most carefully operated upon, double oöphorectomy being done. For a year and a half after castration, normal menstruation continued every twenty-eight days. Upon second operation adhesions were sought and numerous ones found. These had formed about the uterus. Not the slightest bit of ovarian tissue was discovered. Seven months after the second laparotomy, menstruation again occurred.

In my judgment, it is evident that in this case, despite the care exercised in the two operations some ovarian remnant was left which continued functioning. We need only recall the difficulty of finding and differentiating these accessory ovaries at autopsy, working without haste and without hemorrhage, in order to understand the unreasonableness of an operator's arbitrary statement based on a relatively incomplete examination made while operating. Rebaudi, commenting on this case, cites a similar one reported by Gellhorn. But in this a second laparotomy with separation of the uterus from its adhesions put an end to the postoperative menstruation.

External Genitals and Mammae

The external genital apparatus experiences the same morphologic symptoms of *atrophic regression* which I described in spontaneous menopause. In young women this process is usually accomplished so slowly as to allow them a sexually active life up to an age parallel to that of the uncastrated woman. According to my experience certain phenomena are presented very late, the darkening and flaccidity of the labia, the uncurling of the sexual hair and so forth.

The breasts suffer various changes after castration. Often they atrophy. Some remain unchanged (Delbet¹⁵). Some hypertrophy and even secrete colostrum or true milk (Sanger¹⁶). In some animals, such as the cow or goat, castration produces an increase and a notable persistency of lacteal secretion. I recently

¹⁵Delbet: *Semiologia de los órganos genitales*, in Bouchard, *Tratado de Patología general*, Spanish edition, v, 1901.

¹⁶Sanger: *Ueber ein primäres und ein metastatisches Ovarialkarzinom mit Milchbildung in der Brustdrüsen*, *Monatsch. f. Geburt. u. Gynäk.*, 1912.

published cases of sudden cessation of menstruation with persistence of lacteal secretion.¹⁷ But this true parenchymatous hypertrophy must not be confused with the false hypertrophy produced by the accumulation of fat in the retromammary tissue. Pinesse, cited by Carnot,¹⁸ refers to a case of *monthly hemorrhage from the nipple* in a castrated woman.

Leucorrhea and Vicarious Hemorrhage

According to my experience, *leucorrhea* may at times be intense and of periodic course, even monthly, especially in those cases where the uterus has not been extirpated. It is therefore of vicarious character. Various types of vicarious hemorrhages, described on page 129, also have been observed, although with less frequency perhaps than in spontaneous menopause. The fact that they are less frequent may be explained by recalling that women castrated in youth *are not likely to have hypertension*. And, as we know, hypertension is one of the factors predisposing to the various hemorrhagic phenomena.

Circulatory Symptoms. Hypertension in Young Castrated Women

Mention has been made to Paillard¹⁹ concerning the greater frequency of hypertension following castration than in the physiologic critical age. My experience, as has been said, is contrary to his and I cannot, indeed, continue stating as in the first edition of this book that hypertension is always absent in castrated women. But I do claim that *it is much rarer than in the normal climacteric*. Of 36 women castrated before the fortieth year and observed within the first three post-operative years, I have seen only four cases of hypertension, 11 per cent. Compare this figure with those given in Chapter XII—51.4 per cent of hypertensives in the climacteric and more than 10.4 per cent with minimum hypertension.

This absence of hypertension is a further argument in favor of my hypothesis that this symptom does not depend on a lack of

¹⁷Marañón: Op. cit., note (36), page 136. See also a case from my clinic reported by Raguz: Insuficiencia tiro-ovarica y secreción láctea persistente, Archivos Españoles de Endocrinología y nutrición, 1924.

¹⁸Carnot: Opothérapie, Paris, 1914.

¹⁹Paillard: Op. cit., note (1), page 139.

ovarian internal secretion but on a secondary neuroendocrine reaction, which does not appear until the normal date, or perhaps a little before.

For the rest, as in the critical age, *an evident lack of parallclism may be observed between the hypertension and the other symptoms attributed to it like suffocation.* This may be seen in the following examples.

CASE 99.—S. M. A. Sterile; double salpingo-oöphoritis. Total castration at the thirty-eighth year. Fifteen days later suffocation and increase of weight began. These became more marked up to two years later when I saw her. Arterial tension 14.9. Treatment; diet, ovarian extract, etc. *A year later the tension had fallen to 13.8 but the suffocations were even more intense.*

CASE 100.—P. R. Multipara. Always healthy. At the forty-second year severe hemorrhages began, due to a myoma which necessitated total extirpation at the forty-fourth year. The symptomatology began a few days later; not very intense suffocation; pain in the legs, asthenia, nervousness, insomnia. *Tension, 18.9. Treatment; diet, ovarian extract, iodine. Eleven months later she was entirely well but the tension continued unchanged, 18.9.*

Intensity of the Vasomotor Phenomena. Suffocation in Castrates

On the other hand, the vasomotor phenomena occupy an important place in the symptomatology of castration. They are present in almost all cases, and physicians and laity consider these *suffocations* as the symptom representative of ovarian insufficiency. Levy²⁰ has made a careful study of these suffocations of artificial menopause. Its clinical description corresponds approximately to that which I gave a few pages back in describing spontaneous menopause. But perhaps the suffocation in castrated young women is more intense and more typical than in climacteric women. The average duration of the suffocation in castrated women, with its two phases of erethism and sedation, is somewhat longer, perhaps, than in the climacteric, for cases of average intensity. Ten minutes which Levy gives appears to me

²⁰Levy: Op. cit., note (6), page 19.

proper for very severe cases. Lissac²¹ and others speak of hour long attacks which could only appear in the most severe cases.

The suffocations are repeated at intervals varying in length in different individuals. In some patients they appear only two or three times a day, in others more frequently and in very exceptional cases they occur every five minutes.

In castration, these vasomotor phenomena are prolonged during a variable period of time. Schiebele (loc. cit.) gives the average figure of six months to a year as the most frequent. I have seen a woman who five years after operation still had suffocations as violent as ever. According to Levy durations up to ten years are not exceptional, while Lisac (loc. cit.) cites cases in which the symptoms recurred for fifteen years. I recently found another in which it had persisted sixteen, with severe tachycardia in each attack making sleep difficult. Windscheid²² states that there are women castrated in youth in whom the consequent distresses, particularly the vasomotor, continued through life. *I believe that these cases of such long duration presuppose a circulatory state more or less avowedly pathologic.* The heart, arteries, the neuro-endocrine system and certain nerve centers may finally bring about an adaptation of the circulatory system to the new functional conditions created by castration in a period which we may fix at about two years. The woman whom I mentioned as having intense suffocations for five years after operation undoubtedly had aortic lesions. In the case in which flushes continued for sixteen years, the arteries were hardened and the intensity of the tachycardia indicated an unsound myocardium. I have already spoken of the interdependence of suffocation and hypertension.

[I am in entire agreement with the author in his statement that suffocations of long duration are indicative of a circulatory state more or less pathologic. Indeed here we have a situation difficult to manage from the point of view of therapy. Where the suffocations are prolonged and the systolic tension tends to remain close to 200 or above, the case is almost surely one of or-

²¹Lissac: *Traitement des troubles consecutifs à la castration chez la femme*, Paris Thesis, 1866.

²²Windscheid: *Die nervösen Störungen des Klimakteriums*, Zentralbl. f. Gynäk., 1896.

ganic, not functional, hypertension, though the functional upset is present to aggravate the general condition. I have seen cases of this sort in which the hot flushes and sweating were made worse by the introduction into the treatment of ovarian extract, especially that of corpus luteum. Hypertension of this degree has been regarded for some years as rather a contraindication to the use of opotherapy for the simple reason that the suffocations seemed to be best controlled by the ordinary management, alone, of hypertension.—C. C.]

Other Circulatory Symptoms

In castrates there are naturally other circulatory disturbances of a pathogenesis similar to that of the suffocation—like *nervous urticaria* and *simple tachycardia*. On the other hand, *paroxysmal tachycardia* is rarer in young women with sound circulatory organs, however strong the other symptoms of ovarian deprivation may be. But it may appear, as in some of my cases. Again there may be *stubborn arrhythmias* as in Case 35. But the grave circulatory conditions, which I have described in spontaneous menopause, should be exceptional—*acute cardiac insufficiencies, angular phenomena, and so forth*.

Nervous Symptoms. Bone and Muscular Pains

The *nervous symptomatology* which I have described in the spontaneous menopause, may be reproduced almost completely in the surgical. The different *painful phenomena* are frequent, especially these *vague, changing pains, joint or muscular*, which are generally spoken of as rheumatic. Schickele²³ insists on the promptness and relative constancy with which these pains follow castration. In my Case 100 they came on at about the fifteenth day. He also stresses the effects following ovarian therapy. Hence he does not hesitate to consider them as the result of the genital insufficiency.

Headache

Headache is rarer than in spontaneous climacteric, but it does occur sometimes with desperate persistence and violence as in the following case.

²³Schickele: Op. cit., note (14), page 19.

CASE 101.—Woman of twenty-nine; married at twenty-five. Following marriage various genital complaints which gynecologists diagnosed as perimetro-adnexitis. Aggravation despite treatment. Patient's low state precluded cure, whereupon operation was undertaken. Complete uterine and ovarian extirpation. *After the eighth day following castration violent headaches appeared* affecting the right side principally. Great malaise, vomiting, etc. This was repeated every eight or ten days becoming more intense at the time for menstruation. She had no hypertension on the two occasions when I saw her and I do not know if it was present during the attacks. Besides the headaches she had suffocation, nervousness, tachycardia and slight increase in weight. *She was markedly improved by the use of ovarian extract.*

Abdominal Pains

In some castrated women *abdominal pains* are observed. At times these are very striking because of their persistence and intensity. Pende²⁴ cites *hypogastric pains* especially, fixed or radiating to the groin or in other directions. Cabot²⁵ describes a case with *intense epigastric pains*. Here is one of my cases.

CASE 102. C. de P. Forty-two years old. Ten years ago both tubes and ovaries were extirpated as a consequence of salpingo-oöphoritis, probably gonorrheal. Since then various complaints; at first of vasomotor type, suffocation, and later of a principally nervous nature. She had gained eight pounds in weight. The manifestation which most distressed her and which had not varied since the operation was a *permanently painful sensation with marked paroxysms in the hypogastric region*. Nothing was palpated on pelvic examination. She was slightly relieved by opotherapy.

Asthenia. Pruritus. Dizziness. Insomnia

Asthenia is also very frequent in castrated women. Sometimes the weakness is so intense that it obliges the patient to remain in bed almost all day.

²⁴Pende: Op. cit., note (17), page 19.

²⁵Cabot: Op. cit., note (2), page 173.

Pruritus, generalized or local, is also rather common, especially that linked to *kraurosis* and *senile atrophy of the vulva*. Various recent writers, Schickele and those mentioned in Chapter XIII, Graves²⁶ and others emphasized the direct dependence of this upon ovarian insufficiency and consequently its curability through ovarian therapy.

As a manifestation **dizziness**, very close to hypertension, is observed less often in young castrates than in the physiologic menopause.

I have seen cases of **insomnia**, a symptom also mentioned among the usual sequels of castration by Jayle,²⁷ Lissac²⁸ and others.

Psychic Disturbances. Rarity of Loss of Emotional Control

The *psychic disturbances* of castrates are very interesting. In Chapter XIV I described *these elemental psychic changes as loss of emotional control, lessening of libido, sexual melancholy and inversive tendency*. They are strikingly less marked in women castrated in youth since in general neither the endocrine state nor the psychic conditions are comparable to the usual ones in a woman passing through the spontaneous critical age. Thus the state of *emotional instability* which I have just characterized as fundamental in the spontaneous climacteric is less frequent and less intense, less exquisitely perceptible.

Lessening, Persistence, and Increase of Libido

The *disturbances of sexual feeling*, too, are less complicated. *Lessening of libido* is the normal consequence of castration. But *libido may persist*, as it persists in some male eunuchs castrated after puberty. I have already explained that this phenomenon may have two causes; an organic one, the persistence of ovarian remnants or of accessory ovaries which have escaped the surgeon's knife, and second, a psychic cause, the imaginative development of the sexual impulse through the remembrance of

²⁶Graves: Ovarian Secretions, Practical Aspects. New York State Med. Jour., Aug., 1916, xvi, 324, and Jour. Am. Med. Assn., Sept., 1917, lxix, 701, 1917.

²⁷Jayle: Op. cit., note (10), page 335.

²⁸Lissac: Op. cit., note (21), page 340.

preoperative sensations, more like the phenomenon I described on page 332 under the name *erotization of the nervous system*.

Let me mention the cases reported by Tait and Smith of true psychic aberration in women who had been insensible to sexual reaction before operation but who lost this frigidity after.

Peculiarities of Sexual Melancholy in Castrated Women

The state which I have called *sexual melancholy* is the most complicated of the four disturbances in sexual feeling which I have described. It is less frequent and intense in the castrated woman than in the climacteric one. This is because in the castrate there are lacking the psychic elements which have such importance in the appearance of this sexual melancholy. *The sensation of feeling old*, of losing the power for sexual success does not appear in these women. In the majority of cases they conserve almost perfect physical freshness²⁹ and even, as I have said, a false or true but effective sexual impulse. Moreover, in these women castration almost always means liberation from disease, the end of pain and fever, the passage from sickness to health which contributes in large measure to warding off the depressing state of mind and even brings a frank optimism as I have seen sometimes. Nor is the fact of sterility apt to affect the woman's mental reaction much since the women requiring castration are those who are either ill in consequence of abnormal conditions subsequent to pregnancies, and who therefore have had children, or those in whom pelvic disease has already destroyed hope of conception.

Rarity of Virilism. Its Cause

As for the last element in abnormal climacteric psychology, the tendency to *sexual inversion*, the interesting fact is that *it is not observed in young castrated women*. Neither the morphologic changes causing the masculinism described in spontaneous climacteric, nor the parallel psychic transformations occur in women whose ovaries are extirpated in youth. I have never seen it de-

²⁹Bear in mind, that in some castrates the plethoric state and the slight increase in weight consequent to the mutilation contribute to enhance their physical attraction notably.

velop and Kisch, Pende, LeDouble and Houssay say the same. My doubts as to the mechanism of this inversive tendency have already been explained. What takes place appears to indicate that the phenomenon requires a glandular reaction for which the climacteric is propitious. This glandular reaction may be the hyperplasia of the suprarenal cortex as has been stated.

Psychopathies. Loss of Memory

The *psychopathic disturbances, properly speaking*, in artificial menopause have been well studied by Gallois and Beauvois,³⁰ Margolies,³¹ Alaize,³² Delbet,³³ and others. All the complaints which we studied in the menopause may be presented. *Melancholia appears to be the most frequent phenomenon*, with great physical and psychic depression.

Loss of memory, either accompanying *melancholic states* or as an isolated phenomenon is mentioned by all writers. Jayle³⁴ found it 32 times in 41 castrated women. This symptom was very intense in one of my cases and because of the patient's social position it was most obvious and striking.

CASE 103.—X. X. Thirty-eight years old; *actress*. At the thirty-fourth year, following a period of severe local suffering, especially during menstruation, the uterus and both ovaries were extirpated. After castratin she had a short period of suffocation. Then the present state began which is characterized by phenomena indicative of an intense hypothyroid reaction; bloated appearance; slight increase in weight; severe sensations of cold; continuous feeling of fatigue, with attacks of fainting; mental and emotional indifference, and *a loss of memory so profound that the great difficulty of remembering her lines* forced her to retire from the stage.

Every writer has also mentioned the *tendency to suicide*.

³⁰Gallois and Beauvois: L'état mental des ovariectomisées. *Bullet., Medical*, 1898.

³¹Margolies (Mme.): *Troubles psychiques consécutifs aux opérations pratiquées sur l'appareil génital de la femme*. Paris Thesis, 1898.

³²Alaize: *Op. cit.*, note (8), page 19.

³³Delbet: *Op. cit.*, note (15), page 337.

³⁴Jayle: *Op. cit.*, note (10), page 335.

I spoke in Chapter XV of *the influence, at times frankly beneficial, which castration exercises on certain neuroses principally of the hysteric type.*

Postoperative Increase in Weight

Increase in weight is a very common consequence of castration. It occurred in all the clinical histories I have referred to and in fact it occurs in the majority of castrated women. Statistics give different figures as to the exact proportion. Glaevecke,³⁵ for example, found obesity in 42.5 per cent of castrated women and a slight adiposity in 35 per cent. Lieseau³⁶ gives similar figures. On the other hand Jayle³⁷ observed increase in weight in approximately only 25 per cent. The reason for these variations is no doubt due to the difference of opinion as to what constitutes obesity. If only cases with excessive increase in weight are counted, this is, of course, a rare occurrence following castration. But as I said in spontaneous menopause, *ovarian insufficiency does not create obesity but a predisposition for it if exogenous factors operate.* Moreover, in many cases it is not a question of a great increase in weight but of true *qualitative adiposities*, that is, states characterized by special distribution of fat giving the figure a typical appearance. With such a criterion, *adiposity is an almost constant development following castration.*

Fugitive Localized Edemas (Quincke) in Castrated Women

The *fugitive localized edemas*, the endocrino-vegetative pathogenesis of which I have explained, are also presented in surgical menopause. One of my most typical cases was that of a young partially castrated woman.

CASE 104.—H. de A. Without interesting antecedents. Strong emotional etiology, intense and prolonged after her marriage. Several pregnancies close together. Fifteen years after marriage *one ovary was extirpated* because of an inflammation. From that time on she had various disturbances, the most marked being sudden

³⁵Glaevecke: Op. cit., note (16), page 208.

³⁶Lieseau: Der Einfluss der Kastration auf den weiblichen Organismus. Freiburg, 1898.

³⁷Jayle: Op. cit., note (10), page 335.

bloating, at times partial, involving a limb or the face, again total. The edema was soft, pale, and indolent. While the swelling lasted the quantity of urine was diminished although analysis did not show the slightest renal lesion. Blood analysis normal. Nervous state, apathetic. Menses very scanty since operation. Feet and hands always very cold. Diagnosis of nephritis had been made. But I regarded this as a case of *fugitive, localized edema* (Quinke's disease). Instead of the extremely rigorous diet, exercise and massage to which she had been subjected, I prescribed thyro-hypophyseal-ovarian therapy. She improved quickly.

Castration and Painful Adiposity

Dercum's disease, or *painful adiposity*, is also likely to be presented after castration. To the cases cited on page 249 I may add a very typical one reported by Sabatucci and Zanelli.³⁸

Rarity of Diabetes After Castration

Diabetes does not occur in young castrated women. Although, as I said before, the castrated woman is more sensitive than the normal to adrenalinic glycosuria, no doubt this predisposition is not sufficient to give rise to the diabetic syndrome. The probable reasons for this were given in Chapter XVII.

Digestive, Respiratory, Urinary and Cutaneous Disturbances in Artificial Menopause

The *digestive disturbances* which we have studied in the natural menopause may also be presented in the surgical, although not always in the same form. I have already referred to Hernando's³⁹ cases of *hypochlorhydria* in young castrated women, and in the same chapter I described a case of *diarrhea* consequent to castration. The contractural phenomena, *pharyngeal spasms*, etc., may also be observed in these women. Pinesse has described *hepatic congestion* in a woman castrated in mid-youth. This condition was observed by the classic writers in the physiologic climacteric.

³⁸Sabatucci and Zanelli: Un caso de adiposi dolorosa sviluppati in seguito all'ovariectomia. Il Policlinico (Sec. Pract.), 1913.

³⁹Hernando: Op. cit., note (7), page 283.

The influence of castration on the appearance of asthma has already been studied in Chapter XX. Lissac⁴⁰ has described a case of *pulmonary congestion* which occurred in a castrated woman every month, during the days she should have menstruated.

The climacteric pathology of the *urinary apparatus and of the skin* offers no peculiarity in surgical menopause.

Castration by X-Ray

The consequences of castration by the x-ray deserve no special description. They depend on the same circumstances which I mentioned in the surgical menopause, that is, age, previous endocrine and nervous states, and so forth. I shall only point out that slow suppression of ovarian function should have, apparently, an influence toward less intensity in the symptoms. This would be true especially if the hypothesis of intoxication through menstrual retention were certain. This hypothesis was recently upheld by Aschner (page 333). *But my experience is that the symptomatology in these cases of castration by the x-ray is as intense as in those of oöphorectomy. Some manifestations, like suffocation, are even more intense.* This fact, as I said before, may argue against the hypothesis that absence of the uterus is responsible for part of the suffocation phenomenon.

[It has been suggested that the difference between surgical ablation of the ovaries and castration by x-ray may explain the various results obtained by different clinicians. Radiation may destroy only the follicular apparatus of the ovary, leaving the interstitial portion of the organ unaffected. If this can be shown to be the case under certain circumstances, or in certain cases, the argument, of course, must be subject to modification.—C. C.]

⁴⁰Lissac: Op. cit., note (21), page 340.

CHAPTER XXV

THE CRITICAL AGE IN THE MALE

Has the Man a Critical Age?

The first question which arises in studying this last aspect of "*the critical age*" is whether there really exists in the man a period of evolution which may be so described, a period similar to that occurring in woman's life and upon which I have commented at such length in the preceding chapters. Many writers have accepted this idea considering it chiefly from the psychiatric point of view. But others, among them Kraft-Ebbing¹ and Vinay,² deny it. "To establish a menopause," says the first, "for the masculine sex, and to particularize the psychoses which are attached to this age (fifty to sixty years) does not seem to me admissible from either the biologic or the clinical point of view." Vinay adds "the masculine menopause is not a fact. It appears to be rather the result of the imagination of the writers who have described it."

For myself I boldly assert the existence of *the critical age in the male*. Of the "critical age" I say, and not of "the menopause," as Kraft-Ebbing, Vinay and others say. Such an expression implies an initial error since evidently the "menopause," the "cessation of the menstrual flow," is something absolutely alien to the masculine sex. But in this book we have tried to understand the critical age, not as a genital episode, not as an incident of the sexual life more or less accompanied by reactional symptoms on the part of the other apparatus of the economy; but as a stage of organic evolution, perfectly characterized, anatomically and physiologically, in whose center the extinction of active genital life stands out prominently, yet not limited to this genital extinction. The line described by the human organism from birth to death is not suddenly broken into abrupt

¹Kraft-Ebbing: Op. cit., note (2), page 213.

²Vinay: Op. cit., note (12), page 19. Of the recent contributions see also: Juarros, *Climacterio varonil*. *Siglo Med.*, 1924.

descents, like steps. It is rather a smooth, curved line divided into distinct sectors whose limits are not precise. There are three such vaguely defined but actual sectors. One embraces the beginning—infancy. Another takes in the last—old age. Between these, in the middle, lies full maturity. Now between these three sectors there are two others, stages of transition, which are intermediate. In the first the line is inclined toward the fullness of the curve. This intermediate sector is characterized by the appearance of sexual activity—adolescence. The second intermediate sector joins the fullness of the curve to the last sector. With this second intermediate sector the curve of the line begins its descent and this period is characterized by extinction of the sexual function—the climacteric. Adolescence has been rightly called the first critical age, because it is characterized by the same functional instability we have just seen in the climacteric or the second critical age.

The climacteric or critical age is, then, a necessary phenomenon in the evolution of every human being who reaches old age, be it man or woman. The biologic foundation of the feminine climacteric—genital decadence and secondary neuroendocrine reactions—also exist in the male. The different somatic and functional conditions of each sex (detailed in Chapter XIV) explains the clinical differences which the critical episode has in the man and in the woman.

Characteristics of the Masculine Climacteric

The masculine episode comes, indeed, much later than the feminine. It is of more diffuse evolution and limits, as it lacks the menopausal phenomenon as a point of reference. Its organic symptomatology is more attenuated. Its psychologic characteristics are as different from those of the feminine climacteric as the significance of sexual life in man is different from that in woman.

I shall consider first the endogenous and exogenous reasons which justify these differences. Then, from the clinical point of view, I shall detail these symptomatic differences, principally those in the psychic field.

Endocrine Conditions. Testicular Insufficiency

We know that the endocrine crisis of the climacteric is characterized in the woman by ovarian insufficiency and the secondary reaction of the endocrines and of the nervous-vegetative system. *In the man all these organs react in a much less abrupt way. The reactions are milder and have qualitative differences which I shall indicate.*

However, testicular insufficiency, the central part of the masculine climacteric, is produced much more slowly and much later than is ovarian insufficiency. In the majority of cases, in the brief course of a few months the woman passes from full ovarian activity to complete cessation. This occurs within a fixed period—between the forty-fifth and the fifty-fifth year. While in the man, *genital extinction occurs in a more prolonged way and during a much longer space of time.* Very often a man passes the fiftieth year with good sexual aptitude. He may reach seventy, or even exceed that age, with the internal secretion of the testicle intact. I knew a man of seventy-four who cohabited normally twice a week. Cases are frequent where the menopause brings to a wife instinctive and psychic desire for sexual separation while the husband of the same or greater age is still active sexually. Even in cases where the man is unable to perform the sexual act perhaps because of lack of power in the external genital apparatus, difficulty in erection, the internal testicular secretion may not be deficient. The finding of active spermatozoa in the semen of old men up to ninety-one years (Pawloff, cited by Metschnikoff), and one hundred and three (Metschnikoff³), shows the prolonged persistence of this secretion until very advanced ages at which the sexual act itself has become impossible. This finding also explains the frequency with which amorous feelings are kept alive in the very old. This same author recalls that “doctors in asylums for the aged have observed that the principal occupation of the patients is discussion of the love question.” Although, as we shall see presently, in these late manifestations of libido the psychic element takes part in a preponderant manner and not the sexual instinct properly speaking.

³Metschnikoff: Op. cit., note (6) (c), page 205.

Lesser Intensity of the Thyroid Reaction in the Man

The thyroid reaction, so important in the feminine climacteric, is much less marked in the masculine. In woman the thyroid has a functional excitability, a tendency to instability, which it does not have in man. Hence in the latter, the lively and characteristic manifestations of hyperthyroid or dysthyroid background alone or combined with the other glandular disturbances will be lacking. These we studied in the menopause, the violent flushes of heat, palpitations, tachycardia, sweating and so forth. We may expect none of them in the masculine climacteric.

However, climacteric hyperthyroidism may also appear in the male, *being characterized especially by loss of weight and psychic symptoms*, especially the latter. Therefore its possible presence in men of this age should not be forgotten, though always less probable than in woman, in those cases of loss of weight which are generally attributed to neurasthenia.

Suprarenal Reaction. Hypophyseal Reaction

Assuming a suprarenal reaction in the feminine sex, the manifestations which are attributed to it will be encountered and perhaps with equal intensity in the male. These are: 1. *Increase in weight.* The masculine figure loses its youthful grace and becomes corpulent, at first pleasing in appearance, later frankly heavy. 2. *The accentuation of masculine hypertrichosis.* I have found this phenomenon to be almost constant but writers do not call attention to it. On leaving the third decade the beard and mustache are apt to become heavier, but the symptom is manifested chiefly in the bodily hair, on the chest, forearms, and legs. This grows more thickly or appears for the first time in those individuals who did not have it before. *Note that this is an accentuation of masculine sexual characteristics, in contrast to what occurs in woman. In her the glandular reaction (suprarenal?) of the climacteric acts heterosexually, that is, tending to transform the feminine morphology into the masculine.* 3. *Arterial hypertension*, as constant as in the feminine and perhaps even higher in the masculine sex. This may be because the exogenous factors which collaborate in the production of hypertension are more commonly

present in men, such as syphilis, the use of tobacco, overwork and like factors. For these same reasons we are to be guarded in attributing hypertension in women to the climacteric phenomenon alone.⁴

Probably the *hypophyseal reaction* also intervenes in the climacteric crisis in the man. In rare cases this gives rise to acromegalic syndromes, more frequently to the peculiar adiposities with which we are now familiar and which I shall mention again, and perhaps in advanced years to senile atrophy.

Exogenous Circumstances Which Influence the Development of the Critical Age in the Male

The exogenous circumstances are also different in the man. *Certain pathologic processes are more frequently displayed than in the woman. These act preferably on the circulatory system, and, either through that medium or directly, on the nervous system.* Such are some infections, as syphilis, alcoholic or nicotine intoxication, emotional excesses, overfatigue, and so forth, all of which explains the intensity of, and the greater proportion of, insanity as manifested in men. On the other hand, as a consequence of his sexual characteristics, upon which I shall dwell later, man finds this period one of increased possibility through his business or professional activity. This balances and compensates the decline in primary sexual activity. Even after this age the height of man's business or professional activity sometimes persists. Legrand,⁵ to speak of only one of the many examples, mentions those men who, past sixty, arrive at the very peak of their respective capacities. The World War gave us a remarkable lesson as to the social value of old men, of whom, among others can be cited Foch, Joffre, Giolitti, Hindenburg, and Clemenceau. In women, on the contrary, the loss of sexual power implies a radical, physiologic change, as I have indicated.

Peculiarities of Critical Symptomatology in the Man. Genital Symptoms

Thus we see that the symptomatology of the masculine climacteric presents peculiarities as compared to the feminine. The

⁴Zondek: Op. cit., note (17), page 249 expresses the same opinion.

⁵Legrand: *La longevité à travers les âges*, Paris, 1911.

genital symptoms in the man are very simple. The erectile power of the external genital apparatus progressively diminishes until it is completely lost. This is accompanied by flaccidity and slow atrophy of the penis and testicles, darkening of the scrotum, and uncurling of the pubic hair. These phenomena are often effected parallel to a diminution of the sexual impulse and therefore without psychic disharmony. Less often the amorous appetite persists, giving rise to a state of sad resignation in the climacteric man or his instinct goes astray toward more or less complex sexual aberrations. A state of semi-erection may last many years and be adequate for normal, orderly amorous relation. Certain affections of the urinary apparatus, proper to this age such as prostatitis may create a state of local irritation favorable to erectile power and priapism without libido. I have seen some such cases.

Circulatory Symptoms

The *circulatory symptomatology* reveals a fundamental manifestation, *hypertension*. This is as frequent in man as in woman. But, as I have just stated, the characteristically *functional* hypertension without arterial lesion is presented with less purity than in woman. This is because the exogenous pathologic causes so frequent in men, certain infections and intoxications, early produce the hypertensive vascular lesions, which are not apt to appear in the woman until considerably later. *Hence we shall be more cautious than in the other sex in diagnosing these as "functional."*

For the same reason the *complications related to arteriosclerosis* are more frequent in man in the critical age. *Anginal phenomena, apoplectic symptoms* and so forth are favored by the critical plethora.

Xanthoma, Senile Arch and Cholesterinemia

Tests for cholesterine in the blood are likely to show high figures in this age, just as in woman. Often clinical signs may be discovered representing local deposits of cholesterine, such as *xanthoma*, represented by yellowish spots, slightly elevated and localized commonly on the eyelids, and the *senile arch of the cornea* which appears early, coinciding with the hypercholesterinemia.

Rarity of Vasomotor Symptoms

Contrary to the case in woman, *all the symptomatology linked to the vasomotor instability is, except in rare cases, less perceptible in man.* This is true of suffocation. And, considering the frequency and importance of hypertension in man, we find here a new argument against the hypothesis which links suffocation to high tension in the arteries. [But this hypertension in man does not show the *instability* it does in woman.—C. C.] Furthermore the rarity of the hyperthyroid manifestations in the masculine climacteric supports my supposition that a thyroid element enters in the production of that symptom. At any rate, as I said before, the majority of writers, Zondek, for example, include sensations similar to suffocation among the manifestations of the masculine climacteric. I have rarely found them except where there were at times clear hyperthyroid disturbances, as occurred in the following patient.

CASE 105.—S. M. Fifty years old. Had a goiter from his youth. About the fiftieth year this goiter began to be hyperthyroid. When I saw him in his fifty-fifth year there was a hyperthyroid syndrome, not very intense but clear, moderate loss of weight, tachycardia, palpitations, tremor, motor uneasiness, etc. There was, moreover, hypertension with arterial sclerosis. *The principal distress of which he complained was the appearance of severe "suffocations," sensation of heat, flushing of the face, slight vertigo and attacks of sweating.* As his wife graphically said, "It is like what happened to me when the menses stopped, although stronger."

I have seen, but less frequently than in women, *palpitations and paroxysmal tachycardias.* These were presented especially in patients afflicted with neuroses and certain psychoses which I shall explain presently. Even *simple tachycardia* is observed, particularly in cases of hyperthyroidism but always, I repeat, less often than in the feminine climacteric.

Nervous Symptomatology of the Masculine Climacteric

The *nervous disturbances* are very much like those of woman, although in general less marked. Various *neuralgias* present

themselves in this epoch which ordinarily are not referred to the critical disturbance, because in the masculine climacteric there is no phenomenon like the menstrual disturbance to attract the physician's attention. Nevertheless these complaints can be attributed in either sex to the crisis. Generally they are recognized as rheumatic or arthritic symptoms.

One of the cases of *indurative headache* to which I referred in Chapter XIII concerned a man, Case 38. I could cite many more coincident with this age, although less typical than that case.

Also one of the cases given illustrating the typical phenomenon, *painful uneasiness of the legs*, concerned a man, Case 42. He also exhibited various other very intense morphologic and functional changes attributable to the climacteric. This man, now dead, was effeminate and fortunate in his love affairs. Accordingly his organic and psychic reactions were of feminine type, hysteriform—a phenomenon which well corresponds to the Don Juan psychologic complex.

Generalized pruritus is present in a considerable number of men in these years. It is related to latent hyperglycemic states dependent in their turn on the endocrine change of the crisis. See Case 46, for example.

Various sensorial disturbances, principally *ear noises*, *dizziness* and *insomnia*, which I described in the feminine menopause, also appear in man in this age, as Valleteau de Monilliac⁶ has noted. Such cases, however, should be studied more carefully and in greater detail than in women in order to discount whatever may be due to the various organic lesions which might cause these symptoms. Their presentation in this age would be, then, a pure coincidence or an aggravation, through the critical plethora, of existing states.

Metabolic Symptomatology. Abdominal Deformation (Adiposity)

The symptoms of metabolic change are rather similar in both sexes. *Man frequently fattens in the climacteric epoch*, not through an excessive obesity, but rather through increase of

⁶Valleteau de Monilliac: Les troubles nerveux et psychiques de l'âge critique chez l'homme, Thèse de Bordeaux, 1907.

weight more appreciable by the special distribution of the fat than by its quantity. Unlike the other climacteric manifestations, this is apt to appear in the masculine sex as early as in woman. Indeed, on passing thirty and with sedentary habits increased, often the whole masculine figure becomes heavier. A short time later, especially in city men who lead sedentary and unhygienic lives, the abdominal disfigurement, due to accumulation of fat on the abdomen, begins to appear. This, although remote, is the first herald of old age. Abdominal adiposity is an almost constant phenomenon, even in men who remain thin. Generally it is first evident on the epigastrium, gradually extending to the rest of the abdomen which is later folded upon itself in fatty rolls. In some cases these form veritable pendulous overgrowths. In others, no doubt, through the predominance of intra-abdominal fat, the abdomen has an appearance of uniform tension, recalling that of meteorism. On palpation the extraordinary thickness of the panniculus may be perceived. The umbilicus is hidden and surrounded by a roll of fat. In some cases this abdominal fattening comes on suddenly and progresses very rapidly.

Pathologic Importance of Abdominal Adiposity. Circulatory Plethora. "Flatulent Dyspepsia"

I wish to emphasize the importance which this abdominal adiposity, extra- or intraperitoneal, has in the pathogenesis of the mature age of man. In the first place, *it collaborates in a most important way in the production of the serious and frequent circulatory symptoms in plethoric troubles*. Every physician has had experience with these men, almost always between forty-five and sixty, who have large abdomens, plethoric congestive aspect, dyspnea on walking, somnolence, and so forth. Canizo⁷ has described them very well with the name *plethoric cardiopathies*. Now, in the majority of these cases, aside from the lesional element, the fat, which is almost always exclusively abdominal,

⁷Canizo: *Cardiopatías de plethora*. Manual de Medicina interna; Hernando y Marañón, vol. II, second edition, Madrid, 1925. Canizo's practice is chiefly among the farmers and cattlemen of the Salamanca plain. But these adiposities are also very frequent throughout Extremadura and Andalucía. Indeed, there is no region of Spain without this complaint except among the very poor.

plays a large part in the patient's appearance, for normal or even thin legs support a most voluminous trunk. The arms, too, may be thin. The patients themselves are likely to connect the coincidence of their symptoms and the increase in the size of the abdomen. A reducing diet is apt to cure them rapidly, even dramatically.

Asthma, emphysema, chronic bronchitis and like respiratory affections also may begin with the appearance of these adiposities through the mechanism of the abdominal plethora upon which I need not dwell here.

And finally, *abdominal enlargement coincides, especially when the obesity has occurred very rapidly, with digestive distress of the "flatulent dyspepsia" type* so frequent in this period of life. It might be thought that the excessive fat makes digestion difficult in a mechanical way, analogous to what was formerly assumed regarding pericardial accumulation of fat as the cause of cardiac breakdown at last. Meteorism, which causes the "dyspeptic" disturbance, in its turn increases abdominal tension and consequently compression distress. To illustrate the very typical changes in the masculine climacteric I shall give some examples of this syndrome.

CASE 106.—C. de A., sixty-eight years old. Always strong and without disease. Much gymnastic exercise and sports up to his sixty-fifth year. Vigorous physically, sexually and mentally. Very intelligent. He consulted me for an abrupt loss of sexual power which he noted in his sixty-sixth year. *This phenomenon coincided with a rapid increase of abdominal fat.* Abdomen tense. On palpation a thickness of three or four finger breadths of fat could be noted; the umbilicus was hidden. This increase was very rapid and so marked that the clothing of a few months before could not be worn. At the same time, he began to complain of *troublesome digestion, with great production of gas* and respiratory distress after eating. Hypertension. Symptoms of transitory cystitis. Reducing treatment; very notable improvement.

Notice in this case the coincidence of sexual decline, late as it was, with the appearance of ventral adiposity and flatulence.

CASE 107.—A. de G. Fifty-nine years old. An old syphilitic who had had adequate treatment. Very active sexual life. At this age the first circulatory symptoms appeared, dizziness, insomnia because of a beating sensation in the head, coincident with hypertension of 21 (Riva Rocci) which had previously been absent. A short time later he complained of *diminution of sexual power* coincident with such an increase in the *size of the abdomen* that he required new clothing. On examination I found a huge adipose development and some degree of meteorism. *Digestion, always easy, had become suddenly difficult and prolonged with great accumulation of gas*, together with respiratory difficulty which sometimes assumed an asthmatic type. No objective respiratory or circulatory symptom except hypertension. In this case as in the previous one, various urinary complaints appeared due to transitory cystitis and hypertrophy of the prostate. Loss of emotional control. He also presented a psychic state of jealousy toward younger men in his profession, that of painting. This is very characteristic of male psychology in this age, as we shall presently see.

Bear in mind that, in these cases, a possible initial circulatory decompensation may contribute to the production of the flatulence. I have proved this in some instances and obviously it would be another indication for reducing treatment.

Thyroid Loss of Weight in Climacteric Man

Thinness of body, so characteristic of the hyperthyroid mechanism and a very common change in the feminine climacteric crisis, is less frequent in man. *But that it does appear must not be forgotten.* Here are two cases, of interest because they had been wrongly diagnosed.

CASE 108.—Man of forty-five years; always well. A year ago he *noticed he was losing weight*, without his health's being affected. Sleep and digestion continued good, perhaps with more appetite than usual. Four months later *he had lost four kilos.* *The diagnosis was that of beginning diabetes*, but no sugar could be found in the urine. As this showed a slight increase of phosphates, his loss of weight *was attributed to phosphaturia.* A specialist who

treated him for a mild affection of the ear discovered casually a *slight thyroid hypertrophy* and had me examine the patient. Beside the thyroidomegaly, which had passed unnoticed by the patient, I found tachycardia (pulse 106), fine tremor in the hands, sensations of heat, and enormous mononucleosis, 52.6 per 100 mononuclears. Urinalysis revealed nothing important. A year later he was completely well.

Unquestionably the cause of this loss of weight was the hyperthyroidism which spontaneously appeared and was undoubtedly related in my opinion to the age of the patient.

CASE 109.—C. de G. M. Forty-seven years old. Without important antecedents. For a year he had noted a *rapid loss of weight* without digestive cause which would justify it; *nervous excitability*, with great *irritability*, sensation of *palpitation and lessening of sexual appetite*. All these symptoms fitted perfectly into the clinical picture of neurasthenia and indeed such diagnosis had been made. Nerve tonics were of no benefit. On examination I proved the indubitable existence of a hyperthyroid syndrome, characterized by *thinness*, tachycardia (pulse 110), fine tremor of the hands and eyelids, sensations of palpitation, sensations of heat, and insomnia. The *thyroid was slightly congested*. Under treatment of diet, rest, and antithyroid serum he was rapidly relieved. Strangely enough the patient's wife suffered an analogous state of climacteric hyperthyroidism.

In my opinion the climacteric character of the hyperthyroidism in this case is certain. I have seen several cases similar to those just given. They were always characterized by the absence or the slightness of the goiter, the lack of ocular symptoms, the rapidity of the loss of weight without pathologic causes which usually explain it and *without a wasting away parallel to the number of kilos lost*. That is to say, the patient lost weight but the appearance was that of *physiologic thinness*. Moreover, little clinical interest had been displayed in the striking vasomotor disturbances. These characteristics, along with tachycardia and tremor of the hands, enabled me to make a diagnosis. However, we should not forget that this age is also propitious for other conditions which may be manifested by loss of weight as almost the

sole symptom for some time; some of these are diabetes, late ganglionic tuberculosis, leucemia, cancer of the digestive apparatus and kidney disease.

Diabetes. Chronic Rheumatism

Diabetes presents itself in men preferably in this age, but like the majority of other symptoms, later than in the feminine sex, as shown by Rankin.⁸ I have nothing to add, therefore, to what I said of it in Chapter XVII.

Chronic rheumatism appears much less markedly linked to the climacteric crisis in the man than in the woman. But there is a considerable number of cases in which they are associated. As we know, rheumatism is more frequent in the feminine sex than in the masculine. In its chronic form it may appear in subjects with previous endocrine disturbances or in those who at least show certain signs of such disturbance, as *premature whitening of the hair*. I have seen such cases.

Digestive, Respiratory, Urinary and Cutaneous Disturbances

Reference has already been made to the *digestive disturbance* which appears to me to be most typical of the masculine climacteric, flatulent dyspepsia. On the other hand, the digestive upsets related to changes in vegetative innervation, like *irregularities in gastric secretion or of intestinal function*, are not presented in the masculine sex with the intensity, frequency, and chronology which would permit one to relate them to the climacteric.

In studying *asthma* in its relation to the menopause, I explained that this symptom is also presented in genital insufficiency in the man. One of the most typical cases I have given was really a member of the masculine sex (Case 86).

The *urinary symptoms* observed especially in this age and referable in greater or less degree to the sexual subsidence are very few in either sex, although more evident in the masculine. Men who have had disturbances of the bladder are likely to suffer them anew in the critical age, *particularly when, through adipos-*

⁸Rankin: Op. cit., note (12), page 43.

ity and meteorism intra-abdominal tension is much increased, as may be seen in Cases 106 and 107. This is a relation which I have shown many times.

Nor should the fact be overlooked that within the boundaries of this age *complaints of prostatic origin begin*. This is an interesting phenomenon in masculine decadence. Its relation to the decline of testicular internal secretion is very probable, although this point has not been thoroughly studied.

Cutaneous, ocular, and other symptoms are more or less the same as those studied in the woman.

Psychology of the Critical Age in Man. The Emotional Instability of Maturity

I have intentionally kept for the last a consideration of *the psychic sphere*, because here we find the symptoms which especially characterize the crisis of the sexual subsidence in the man. Following my method of commenting upon these manifestations in the feminine menopause, I shall consider first the "*elemental psychologic disturbances*" of the climacteric, and later the *psychopathies properly speaking*.

Emotional instability is a frequent characteristic of the psychology of man in this age, only it is presented with rather less intensity than in woman. In her the reactions dependent on the endocrino-vegetative system are always more violent, at least in their external expression. The emotional sphere of man has apparently been rendered dormant by his struggle for existence, but at this age he is apt to reach his maximum emotional susceptibility. Such men have told me that they were now moved emotionally by things to which they were formerly indifferent.⁹ Great fighters, of little sentiment in the early part of life, become gentler, more understanding, and indulgent in the period of de-

⁹In my essay on Age and Emotion I referred to this phenomenon in speaking of woman's climacteric loss of emotional control. There I copied these lines, more expressive than any description, from a letter sent me by a well-known writer who was rounding the cape of the fifty-fifth year in rough weather.

"My eyes fill with tears, a sob escapes me, my throat tightens easily now, only on seeing a child, hearing a musical note or seeing a misfortune. Now I move my hearers when lecturing, for my soul is hypersensitive through force of suffering, deception, and struggle. And from this exaggerated sentimentalism I gather much deep consolation."

cline. Maturity is also the time for the conversion of great sinners.¹⁰ And to this the climacteric instability of the endocrino-vegetative emotional system contributes very largely.

Climacteric Impatience, Instability in Man

Impatience, becoming easily exasperated, is a very frequent sign of loss of emotional control in the climacteric man, as in the woman. Many men of uniform and tranquil character throughout life become impatient, irritable, and violent in this age. The usual little cares of the home or profession which before were scarcely noticed, now constitute a torment. This change is readily perceived at home and abroad. The explanation of the phenomenon is always the same, emotional irritability. Naturally the psychic states related directly or indirectly to sexual decadence have a large influence upon the characteristic irritability of some men in this age.

Disturbances of Sexual Feeling. Pathologic Lessening of Libido

The *disturbances of sexual feeling* properly speaking are less interesting than in the feminine menopause, for the reasons so often explained. The *lessening of the sexual impulse* rarely reaches pathologic limits, being brought about in a more gradual manner with less shock than in the woman. It also occurs much later. I did see, however, a patient who, on reaching fifty experienced an almost abrupt loss of libido with voluntary renunciation of all sexual relation. Here is a state similar, although with

¹⁰In proof of this note the frequency with which conversion coincides with an emotional state, either a sudden and exciting emotion, like Paul's vegetative terror at the lightning during the tempest, or the Duke of Gandia's sentimental horror on seeing the Empress Isabel converted into a hideous mass. It may be gentle, like an altruistic action or spiritual words, or merely solitude in a beautiful landscape. Such was the critical moment of St. Augustine's conversion. About the year 386 he stood—after an unfortunate youth—upon the threshold of maturity. Following a period of internal struggle which not only agitated his spirit but also his body, "animated by unfamiliar emotions" he fled to solitude and "being under a fig tree" beneath the Italian sky in the latter part of autumn he suddenly felt "two streams of tears gush from his eyes." St. Augustine, so attentive to the details of his inner life, makes no allusions in all his *confessions* to nature other than this detail of the fig tree. Here we find revealed how emotions inspired by nature about him was linked to his spiritual crisis. This feeling inspired by nature is one of the finest and most suggestive possessed by the human spirit and serves as a stepping-stone to important emotional states.

more marked intervention on the part of the purely psychic elements, those which I described in previous chapters as occurring in women.

Rarity of Sexual Melancholy in the Man

The symptom which I called *sexual melancholy*, so complex and so interesting in the other sex, is of very little importance in man. Organically the depressive commotion which causes the suppression of the genital hormones is less in the man than in the woman, since in him the primary genital function is less important than in her. Moreover its extinction is accomplished in a less brusque manner and covers a much longer period of time. Nor is the loss of sexual power apt to be followed psychically by the depressive states which are observed in the woman. This is because of the lesser significance which this loss has in masculine psychology, and because it coincides with the fullness of business or professional activity. This not only is an efficacious consolation, but, according to my way of thinking, represents a certain kind of sexual (parasexual) satisfaction in the man.

The states of "*sexual melancholy*" are, then, very rare in normal climacteric man. We find only isolated examples, in those subjects of Don Juan temperaments. These I consider as of ambiguous sexual psychology.¹¹ I might mention two or three cases which I have collected of true melancholia in the face of physical ruin in men of this sexual context. I copy as typical a description taken from a novel by E. Montfort¹² which is scarcely true literally, but very interesting from this point of view. The hero, a ladies' man, surprised and disillusioned on entering his fortieth year meditates thus: "Forty years! He was forty years old! His age was written in every bit of him, in the flabbiness of his face, in the heaviness of his body, while his heart, not aged but still young, beat as though it were at its twenty-fifth year. Forty years! Pleasure was ended, no longer could he interest women.

¹¹See my essays; (a) *Notas para la biología de Don Juan*. *Revista de Occidente*, Jan., 1924; (b) *Nuevas notas sobre Don Juan*. *Tobogan*, No. 1, July, 1924. I am preparing a detailed explanation of my ideas on Don Juanism. In this I shall explain my point of view on normal and pathologic sexual psychology which in the present book appears rather scattered. At the same time I shall reply to some criticisms of my earlier essays.

¹²E. Montfort: *La belle-enfant ou l'amour a 40 ans*. Paris, 1918.

Having reached the end of youth, having passed the time of love, what pleasure in life now remained to him? The obsession of the lost paradise, the thought of things past, the ever present memory of the enchanted country where he had once been and whither he can never more return! All is lost at this age." And later: "He beheld himself in a mirror. The image was terrible. Impossible to retain the least illusion that he was the same being. He saw the whole disagreeable transformation, his wrinkles, the crow's feet they had made in his cheeks, the flabbiness of his skin, his thick neck. He was withered, worn out. He was old. Fifteen years before he had seen a man of about this age go out of the house and he now recalled exactly the impression which he had produced, the painful sense of physical ruin, a pot-bellied being in a shirt, disheveled, his eyes swollen, his legs hairy. The spectacle had been grotesque and lamentable. And now he himself was like that man."

The lamentation of this Don Juan, evidently abnormal in his sexual makeup, could not be less masculine. The author adds later with a certain sagacity, "He was inconsolable. Stronger men, less effeminate characters, those whose existence is more active, accept physical decadence. They pay some attention to it. They suffer, perhaps, upon the appearance of the first wrinkle, when the first hair falls out, when abdominal fat begins, but they suffer in only a transient way. By the side of loss they can write gain. Maturity of spirit, more complete possession of themselves, intellectual and moral benefit compensate them for the physical loss."

The Age of Love in the Modern Man. Social Well-being as an Element of Sexual Attraction

The abnormality and the rarity of these forms of sexual melancholy in the man are accentuated in modern times. It is evident that in present-day society, correctly reflected in the amatory conflicts of contemporary drama and fiction, the lover is of a more mature type than were the gallants of the classic and romantic eras. Toulouse¹³ says truly, "around the age of forty,

¹³(a) Toulouse: *La question sexuelle et la femme*. Paris, 1918. See also:

(b) Voivenel; *La crepuscule de l'esprit*; *Mercure de France*. Mar. 15, 1924. He cites numerous modern books wherein the hero is very mature.

the age of gray hair wherein Moliere's Arnolphe became ridiculous to the ladies, our contemporaries have made the greatest distraction in the feminine heart." "In the theater of today," he adds, "the 'young gallant' is frequently a man in the close of life."

The backward transition of the age of love in man is due to complex causes which I cannot develop here. On one side, it is evident that humanity has taken into account that the concept of youth which has been accepted for centuries—or to put it better, the granted supremacy of youth—rests on entirely superficial foundations, and this concept is beginning to be rectified. The young man is, no doubt, more handsome, more agile and has neither wrinkles nor gray hair. He bears certain physical attacks with difficulty and as yet has not the idea of responsibility which sharpens the actions of the mature man. But none of this upholds the essential superiority of youth. The genital function, subject in youth to weaknesses dangerous at times to later life, does not reach its full stability until the thirty-fifth year or later. Resistance to physical work and above all to intellectual work does not reach its maximum until about fifty. The amount of rest required by youth is less and material necessities much more limited. Emotional life is, as we have seen, of very late apogee, and intellectual control is also fuller and more refined when the youth comes to bear a considerable number of years upon his shoulders.¹⁴

Why, then, has this overwhelming superiority of middle age in the noblest human activities not created a concept of a "golden age" which should depose this present concept based on purely morphologic elements? It would be most interesting to investigate why youth has maintained itself for so many centuries as an age uniquely desirable—and does so continue in spite of changes which are beginning.

¹⁴This statement is not incompatible with the theory sustained by many writers and particularly by Ostwald in his well-known volume *Les grandes hommes*; (Dufour's French edition, Paris, 1912) as to the precocity with which the majority of great men are apt to produce the fruits of their genius. Besides these early geniuses there are late ones like Cervantes, Pasteur, and many others. Moreover, discovery and invention, which is what Ostwald refers to principally, is often favored by impulsive activity, by the very lack of critical talent in youth. But the whole work, developed, clarified, and conscious, the work rather of pedagogy and social diffusion—, is apt to be late even in these precocious inventors.

I have discussed this elsewhere at a length improper here. But I may point out that youth's panegyric has been written since the beginning of the world by the old. And the old do not weigh the advantages and the inconveniences of each age at their individual and specific value; but rather in their relation to a phenomenon which, consciously or unconsciously, is projected upon human thought since it ends it—death. When youth is extolled over the years which follow, it is not youth in general that enchants us but our own lost youth. It is not the vigor, the joy, the youthful freedom from care for which we envy this age. It is rather the mere fact of its being the farthest removed from our own death. If human life developed inversely and the mature man dissolved like a snowball melting in the sun, to end in the unicellular germ, who can doubt that these same longings, now applied to youth and childhood, would be applied to maturity and old age?

But when the value of each stage is judged without this unconscious projection of feeling toward one's own life, then certainly youth is not the most to be desired. A man seeking a collaborator in the most noble human enterprises, one to direct people or industries or financial projects—the sick man seeking a physician, another seeking a counselor—all value maturity above youth. When the young achieve these high positions it is because a premature equilibrium has enabled them to reach the excellencies of maturity aforetime. And this same criterion, this preference for the more mature may have an influence in the choice of a mate.

The fact is that the incidence of marriage between young women and men already mature is constantly increasing. A large majority of women agree with the line of thought expressed by Perez de Ayala:

"A man's heart does not acquire full capacity for love and for every delicate or passionate sentiment until between the fortieth and fiftieth years." "Then man is more seductive than at any other time."¹⁵

It is clear that in the phenomenon we are discussing there is doubtless a material motive, whose consideration we should not

¹⁵Perez de Ayala: *Op. cit.*, note (46), page 152.

overlook. Of course the mature man's economic and social position is stronger, or at least better assured, than it was in his youth. How then, shall we judge a woman who "marries for money," in the common phrase? I believe that we should be far less severe than society, hypocritically, has been. I leave out of consideration those women who, violating every emotional, moral and esthetic sense, marry degenerate, physically repugnant men, whom they despise, solely for money. These we need not consider. But the woman who, on feeling intensely drawn to a man, reflects on his poverty and even lets this fact weigh heavily in her decision, is she as contemptible as these others? I say no. A man's social status has a sexual value, as I have already explained. His business or professional success is therefore a means of sexual attraction. Money, like glory, is the practical expression of that success. Therefore the influence which a large fortune, like that of social position, exercises upon a woman seeking a mate may be adjudged a legitimate biologic means of attraction. Often, as we know, money does not represent any social success, being merely an inert inheritance. But even so the possession of a large fortune gives a certain social preponderance, secondary but unquestionable. To triumph one must be rich. But being rich one may triumph easily. In every case the possession of money is a necessary element to fulfill the fundamental instinct for maternity. It may not have been so formerly, but it is so now and money is becoming more and more necessary. Gold now approaches the class of elements which are not yet of primal necessity but which are radical, biologic necessities like health. A woman may be a mother without money, as she can be a mother without health, but in an imperfect way. These ideas, which I developed in the first edition of this text, are becoming more commonly accepted. There is an extensive social justification for them as the economic difficulties of life become more acute. Prevost,¹⁶ in a recent study of the present-day woman,

¹⁶M. Prevost: *Nouvelles lettres à Françoise ou la jeune fille d'après guerre*, Paris, 1924. In fact Schopenhauer (op. cit., note (21), page 213) sustained this same thesis in commenting on the Spanish proverb "who marries for love must live with grief." "The contrary happens," he says "when we consider marriages of convenience, governed by family interest." Schopenhauer, however, was mistaken, in my opinion, in assuming that money is prejudicial to the species. On the contrary, the species is just what gains when there is no lack of money in the home. The woman who marries for money sacrifices her own happiness for the good of her offspring. The great philosopher of Dantzig re-

exactly expresses these ideas in the words he puts into the mouth of a young woman. She had repulsed a man who was pleasing to her on being informed that he had no fortune:

"Nothing I said is extraordinary. If I knew there was an hereditary disease in his family, however little it was his fault, everyone would find my coldness very natural. The lack of fortune is likewise a tare among the wheat. He is somewhat incomplete and unsound. This is the way I think—and many others do, too."

Economic equilibrium, then, becomes a point of sexual attraction. And in general, this equilibrium is reached only in post-juvenile years, when the chronologic field of masculine sexual suggestion is considerably widened.

This inclination of young women toward mature men at times finds a corresponding phase in the attraction which young women have for many men who have reached the age of sexual subsidence. I have expressed the reasons for this in Chapter XV and shall return to them again shortly.

Man's Feeling of Being Left Behind Socially, Equivalent to Sexual Melancholy in Woman

But on the other hand, in the climacteric man there is frequently a psychic state which we may consider as equivalent to "sexual melancholy" in the woman. This is *the sense of being ill-used, left behind or prematurely forgotten* by the coming generations. This psychic state which embitters the existence of many men in the decline is presented as a plain psychopathic manifestation in varying grades from simple worry, compatible with normal conditions, up to true states of *persecutory delirium*. It may be combined with psychopathies properly speaking—melancholia and so forth, which I shall consider later. Each age has its place in life. The same is true of sexual activity which is as important in woman's life as social or business activity is fundamental in the sexually balanced man's life. Normal men and

marks that in that analytic glance with which young men and women scrutinize each other on meeting for the first time there is felt the genius of the species which is evaluating each. Now no doubt there enters into the meditation of this genius along with a consideration of the psychic and physical qualities of the possible lovers a gauging of the economic resources of each.

women keep this in mind and adapt themselves naturally to the passing moment. But if the nervous system is unbalanced by the rude struggle for existence or by previous diseases, on reaching the critical age with its exquisite emotional sensitiveness the spirit rebels in the face of the natural descent. In the woman this rebellion gives rise to "sexual melancholy" and in the man to its biologic equivalent, suspiciousness in the presence of the natural advance of youth which is always turbulent and iconoclastic.

Evolution toward Conservatism

In this connection it is curious to note the evolution toward conservatism which normally occurs in the man in his social activity the sexual character of which I have so stressed. Man's social activity results from the counterposed action of two orders of impulses, one excitant, the other inhibitory. This is true, indeed, of all organic functions. Now many of these functions, like metabolism, growth, sexual libido, and so forth, in the course of life undergoes a rather fixed evolution which is characterized by the predominance of the excitant elements during youth, by their balance during middle age, and by the predominance of the inhibitory elements during organic decline. Social activity, despite its complexity, follows a parallel evolution. In youth the impulses which we may call centrifugal, are altruistic, correspond to the impulsive, unorganized intellectual power and to the lack of autoeriticism and the aptitude for those emotions I have called "epic" or of "large vibration." These are the impulses which give rise in science to great discoveries, in art to reformations frequently and in politics to advanced policies and propaganda. These movements are considered by contemporaries as revolutionary. But when this age passes, and parallel to the evolution of the metabolism and the organic morphology itself of the different general functions, then the inhibitory impulses, centripetal, egoistic, begin to prevail over the centrifugal. The sense of responsibility is increased, the affectivity is sensitized to the "lyric" emotions or those of "small vibration." The man, in short, whatever his occupation tends to strip from his work the audacious and aggressive character of youth. He becomes

conservative. In studying humanity one of the most conspicuous things is the unfailing repetition of this phenomenon of conservative transformation in each individual and in each generation, always provoking the same surprise and protest from the rising generation. This evolution is regarded as a childish desertion due to egotism or as due to organic decadent diffidence. It is not seen to be the inevitable course of a complex function as linked to the evolution of the individual as are the more simple vegetative functions. Nor is it ever thought to be probable that we all shall follow a like evolution which has gone on repeating itself without interruption as far back as man has a history.

Of course in stating that an evolution toward conservatism occurs in every individual I am not speaking in a strict sense. There are, indeed, men who remain innovators in social activity up to very advanced age. There are many examples of artists, scientists and statesmen who accomplish their revolutionary work after fifty, at times in full old age. But these are always geniuses, exceptional men. Moreover, in these it is easy to show the presence of an uncommon organic energy and, above all, a persistency of sexual activity which exceeds the law of time. These demonstrate nothing contrary to my thesis. The inhibitory conservative impulses do not appear until very late because sexual evolution, the axis of the principal functions, is very late.¹⁷

Pathologic Increase of Sexual Feeling. Disharmony with Genital Capacity and Its Consequences

Pathologic increase of sexual feeling is rather frequent in the climacteric man. In general it assumes different forms than in woman, since not all the organic and psychic reasons which explain the frequency of this pathologic condition in climacteric woman are applicable to man. In the latter it is almost exclusively a phenomenon of purely psychic origin and nature. *Its characteristic is disharmony between the increase of sexual appetite and the diminution of power in the genital organs.* Men are rare in whom libido does not survive erectile power. This lack

¹⁷Likewise, in any class of activity conservatism in youth is an indication of a precarious vital energy, of a premature spiritual senility when not due to a conscious attitude.

of parallelism between the impulse and the functional capacity does not exist in woman because of her passive attitude in the sexual act. But in man the active element is very important. In this phenomenon should be sought the cause of many psychosexual phenomena of masculine maturity. Such are, for example, the *abnormal, perhaps aberrant, forms of sexual gratification*, the attainment of which forces some to break the calm rules of their usual life. The most frequent of these abnormal forms is the *gerocomic tendency*; that is, desire for very young girls. At times this reaches grades of pathologic intensity, of true exhibitionism in men of previous circumspect habits. I could cite various personal observations of this tendency in individuals, some of whom have acquired newspaper notoriety.

Another Consequence of This Hypersensual-Hypogenital Disharmony; the Social Submission of Man to Woman

Another very interesting effect of this disharmony is the *social submission of man to woman*. The sexually normal man walks through life at his own pace, followed by the woman. His respect for feminine will is limited to the occasions when he has to overcome the resistance of the woman to the primary sexual act. But, except within very narrow limits, does her sway extend to his life beyond this circle. *Outside the home no normal man is the slave of the woman*, however ardent and secure may be the spiritual and passionate tie which unites them. This does not exclude, naturally, the reality of a certain feminine influence always useful and agreeable in special moments in the struggle for existence.¹⁸ What I have said in Chapter XIV and again in this one regarding the psychology of sex justifies this statement, while an intimate study of men confirms it in every case. When a man is moved throughout life by the insistent influence of a woman, it is evident that his sexual equilibrium is not perfect. This is absolute when his specific hormones are weak, his genital apparatus defective, or it is relative when the excessive energy

¹⁸This influence, of secondary type, is founded in part on the value of feminine advice. Woman's conservatism and practical advice well balances the idealistic exaggeration of the man's social efforts. And in part the influence is due to the agreeable voluptuousness which the strong feel in submitting to the caprices of the weak. To this same phenomenon is due the domination of children who at times, as in so many sentimental tales, conquer men of indomitable will and character.

of the heterosexual hormones in the woman react on him. Naturally the practical consequence of this disequilibrium, submission in the man, reaches its greatest strength when there is a tie of intense affection on his part which maintains the union with the woman. Such is the case of some men sexually normal during previous years, who on reaching this age of sexual subsidence are urged on by a determined woman, through a psychic exacerbation of the sexual sentiment. Here is the psycho-physiologic conflict favorable for great submission on the part of the man. It has been during this age that the greater number of women who have influenced history, not through their own direct acts but through the instrument of some statesman, have found men docile to their suggestions. A representative type is the well-known hero in Bernstein's *La Griffe*.

Absence of the Heterosexual Tendency in the Critical Age of Man

As we have seen, in the endocrine crisis of the masculine climacteric the *tendency to sexual inversion*, so common and typical in the feminine, is much less frequent. In nonpathologic conditions, revivification of the heterosexual secondary characteristics does not occur with the same regularity as in woman. But at times, on the contrary, there is a reinforcement of masculine characteristics. For this biologic reason the inversive tendency, likely to occur in the climacteric woman, does not have so great an importance in the crisis in man. However, late manifestations of homosexuality may coincide with this period of life, at times leading to manifestations which are scandalous. It is possible that the predilection for very young women felt by men in sexual decadence, the "gerocomic tendency" of which I spoke, is really a dissimulated homosexual inclination localized in the ambiguous, androgynous type of girl very close to puberty.

Psychopathies Properly Speaking

The *psychopathies, properly speaking*, of the masculine climacteric have been well studied by Dubois,¹⁹ Skae,²⁰ Bombardo,²¹

¹⁹Dubois: Les Psychonevroses et leur traitement moral, Paris, 1914.

²⁰Skae: Folle climacterique chez l'homme. Dublin Med. Jour., 1865 (cit. by Vinay.)

²¹Bombarda: Menopause virile. Revue de Psychol, 1899.

Valleteau de Monilliac,²² Mendel,²³ Hollaender,²⁴ and others. All agree that in man, as compared to woman, these are apt to be of greater intensity, doubtless because of the greater frequency and energy with which toxic and venereal infections act, directly or indirectly, through the medium of the circulation. For the rest, the description I gave in considering the feminine menopause (Chapter XVI) is, with the exception of the usual pathologic differences in the sexes, applicable to man.

The most characteristic affection is *involutional melancholia*. This is presented with considerable frequency in climacteric man, with all the characteristics I have described and with its varying termination, favorable in some cases, unfavorable in others. Perhaps the latter is more frequent than in women, through its readier continuity with the arteriosclerotic dementias.

The different *paranoias* mentioned as occurring in women are also presented in the other sex. Cases of religious delirium are not rare. I have seen several very typical cases in some of which the men stood high socially. The same is true of *sexual deliriums and aberrations, persecutory delirium, pathologic envy*, and so forth. All these states are the prolongation of the psychic abnormalities which we have studied in the preceding pages.

Neurasthenia and the Critical Age in Man

Among the neuroses, neurasthenia has been described, chiefly by Regis,²⁵ as very frequent and persistent. But now we know that many of the cases so diagnosed are, as I set forth in speaking of the feminine neuroses, true states of involutional melancholia or of the initial disturbances of presenile dementia, as Regis states.

But in other cases the condition is really *genuine physical and psychic exhaustion*, the "run-down" state as it is phrased, corresponding to the old idea of neurasthenia, without psychopathic disturbance properly speaking. Yet this state corresponds to the psychologic characteristics of the climacteric which have already been enumerated. The symptoms are quieted by rest, but quickly

²²Valleteau de Monilliac: Op. cit., note (6), page 356.

²³Mendel: Die Wechseljahre des Mannes, Neurolog. Centralbl., 1910.

²⁴Holländer: Die Wechseljahre des Mannes, Neurol. Centralbl., 1911.

²⁵Regis: Op. cit., note (1), page 197.

reappear on the least physical effort and especially on any mental or emotional effort. They are aggravated after cohabitation and are accompanied often by hyperthyroid symptomatology which slowly but finally disappears. I have seen several cases coinciding exactly with this description. As characteristic I copy a clinical history, written by the patient himself.

CASE 110.—A civil engineer. "I am fifty-six years old. I have always been well, thin and very nervous. I have worked a great deal in my life, and I was passionate about everything, important and unimportant. A year ago I went through a long period of professional worry and annoyance and a little later I began to lose weight without cause for I ate and slept well. Digestion was good. Without knowing why, I was better for some months and regained the lost six kilos of weight. But suddenly I lost them again. They suspected I was diabetic but the urine was always normal at every analysis. At the same time that I lost weight I experienced my nervous disturbances. So sudden were the severe prostrations, so alarming, that I remained in bed all day—they were like nervous excitations. At times the weakness in my legs made me think I was going to fall, that I could not get out of bed. But I rose and by an effort of will went out and worked. It often happened that by night the weariness left me and I worked until dawn. Some days I could only crawl to my office but left it sprightly—as if my body weighed nothing and I were twenty. There were days when everything irritated me and angered me. I do not see how the members of my household and my companions endured me patiently. I also complained of pains like rheumatism, in the sides and shoulders—every day in a different spot. I slept well but before I went to sleep my head and heart throbbed."

Examining the patient some time later I observed: thin type, eyes large and brilliant, tachycardia (pulse 100-110), great vasomotor irritability; great vehemence of movement and expression; hypertension 19 (Riva-Rocci), tremor of the hands, reflexes heightened and symmetrical. Circulatory apparatus and respiration normal. Syphilis, negative. Two years later he was well. Evidently this subject had a constitutionally hyperthyroid tem-

perament and on reaching the climacteric years he suffered an increased hyperthyroidism. This, with the hypertension and vasomotor reactions of his age, produced a condition of physical and mental asthenia with very marked irritability, the classic neurasthenic type.²⁶

However, I would insist upon considering with caution the psychopathic disturbances of this age as being purely functional or psychic and linked to the climacteric episode. My experience of the last few years has taught me that even in those cases most easily fitting the typical description of climacteric states, *even in those in which the symptomatology disappears and mental integrity is recovered*, there are often pathologic lesions linked to the arteriosclerotic psychopathies. Indeed, after some time somatic signs of arteriosclerosis reappear, at times with greater intensity, it being possible to prove them in the intervening periods of apparent recovery. This does not authorize one to say, perhaps, like Bleuler²⁷ that the so-called climacteric psychopathies should be eliminated from psychiatric terminology but rather that we should modify our concept and prognosis of them. I may sum up my belief in this respect by stating that the climacteric has an influence on the chronology of presenile and senile psychoses perhaps through the circulatory and toxic reaction which presumably contributes to their production. But it has no other influence.

²⁶Vorvenel (Op. cit., note (13b), page 365) cites P. Margueritt's observation of himself. In his novel *La Flamme* he refers to his own climacteric melancholia, which is, indeed, very typical. He mentions other men of letters who, at fifty, are overtaken by a condition of asthenia and disenchantment causing them to shun society and at times to break off their literary labors (Shakespeare, Racine, Huysmans, D'Annunzio). These attacks may be considered as climacteric exhaustion (run-down condition) except when they were theatrically premeditated.

²⁷Bleuler: Op. cit., note (6), page 218.

CHAPTER XXVI

TREATMENT OF CLIMACTERIC SYMPTOMS AND CONDITIONS

(A) BASIC TREATMENT, REJUVENATION, OPOTHERAPY, GENERAL HYGIENE AND DIET

Is Therapeutic Rejuvenation Possible?

The astonishing experiments of these last few years have established the possibility of realizing therapeutic rejuvenation by ligating the epididymis or the vas deferens in man or by ovarian roentgenotherapy in woman, or by transplanting the genital glands of apes.¹ This being true, treatment of the pathogenic type of menopause would be by means of such procedures. But in reality what can the man or woman in sexual decline hope from all these interventions? I recently considered this point² which I cannot detail here. But I may state my opinion. The effects achieved by these operations are limited to a passing reactivation of a sexual function which was languishing, and to an equally mild and transitory reanimation of the general state. And in this improvement in both the sexual and general conditions there must be considered the extremely important part played by psychic factors, to which normal and pathologic sexual symptoms are so responsive. The experimental and anatomico-pathologic work, which serves as basis for these studies, justifies the belief that a certain improvement in sexual function may result. Cardenal's technic, which precludes a psychic influence on the part of his patients confirms this. When operating for hernia in the old he ligates the vas without telling the patient. But all this is very far from what may be called "rejuvenation."

¹See the bibliography on page 31, notes 20-25 incl. and page 186, note 2. From the clinical point of view see; (a) Cardenal's wide experience, *Sobre el rejuvenecimiento. Discurso de entrada en la Real Academia de Medicina*, Madrid, 1923; (b) Voronoff; *Quarante-trois greffes du signe a l'homme*. Paris, 1924; (c) Lipschutz: *The Internal Secretions of the Sex Glands*, 1924.

²Marañón: Comment on Cardenal's article, mentioned before and op. cit., note (11), page 54.

Nor does even a "partial rejuvenation" follow. As Pütter³ says, "It is rather a sham rejuvenation." Man may, as I said elsewhere, by means of these operations, delay with his finger the hands of the clock, but it is futile to cherish illusions about such an act. The clock's machinery continues marching on inexorably within its case. The positive and indisputable, although precarious, advantages are concentrated precisely upon the sexual function. Thus we may say that the real indication for these operations is not senile decadence, which represents a complete decay of the organism, but the climacteric wherein sexual decline is itself almost complete. For the present, I repeat, the paucity and inconstancy of the results collected do not authorize the recommendation of these operations, except perhaps in very special cases in which they may fulfil a psychotherapeutic indication.

In women with surgical menopause necessitated by inflammatory or neoplastic disease, ovarian grafts may be indicated in exceptional cases. But as Tuffier and his associates have established,⁴ and further progress in technic has not improved the results, the benefits are temporary, since the graft is finally absorbed. Sudden and premature menopause may also be an indication for ovarian grafting. But here too the same end-result, ultimate absorption, obtains.⁵

[There are but two definite proofs of ovarian efficiency; one is menstruation and the other is pregnancy. With the preservation of the uterus, ovarian grafting, as in Bell's experience, has been shown to be successful. With ablation of the uterus, however, the absence of vasomotor disturbances following ovarian grafting at the time of the original operation may be due to the grafts having fortunately taken, but this is always doubtful because a certain proportion of women are free from suffocations, anyway, during the climacteric, surgical or spontaneous. Autografting is well worth while in young women, but with homolografting I have had no appreciable success whatever.—C. C.]

³Pütter: *Op. cit.*, by Zondek, H.: Note (17), page 249.

⁴(a) Tuffier and Vignes: *Etude anatomique de quatre greffes d'ovaire chez la femme*. Soc. Anatomique, 1913.

(b) Tuffier, Gery and Vignes: *Etude anatomique sur l'involution d'une greffe d'ovaire*. Soc. Anatomique, 1913.

(c) Tuffier: *Les greffes d'ovaire*. Acad. de Med., 1913.

⁵L. Recasens: *Un caso de amenorrea tratado por opoterapia*. Soc. Ginecologica Espanola, 1918.

Ovarian Therapy. General Indications

The study of *ovarian therapy* takes in various points; the *indications, choice of preparation, form of administration, and the results* obtained by its use.

The indications for ovarian therapy in the critical age are reduced to these:

1. *From the time that the first climacteric symptoms are initiated up to the time they disappear, ovarian medication is indicated in all the symptoms and incidents related directly or indirectly to the crisis.*

2. *Whatever other medication is indicated by the nature of the climacteric symptoms, as for example, circulatory tonics or nerve sedatives, is compatible with ovarian medication and should be associated with it.*

I know of no contraindication for the use of ovarian therapy.

Within these general bounds, it is clear that ovarian medication will have an especial indication in those disturbances which are more directly linked to ovarian insufficiency. I said at the beginning of this book (page 79) that a climacteric woman may present three classes of symptoms. In the first group are those whose relation to the climacteric is merely chronologic. In these, of course, it would be useless to employ ovarian preparations.

In the second group, composed of symptoms not dependent on the crisis but which are aggravated or thrown into relief by it, ovarian therapy associated with the remedies which the various etiologic factors indicate will obviously be useful. For example in the circulatory aggravations of the crisis ovarian substance associated with cardiac tonics is logically indicated.

In a third group finally are the manifestations directly dependent on the climacteric crisis. Here, therefore, lies the chief indication for ovarian therapy and consequently here the maximum of success in its use is found.

Choice of Preparation. Partial (Luteinic) or Total Extracts

A point of great practical interest is that referring to the choice of *opetherapeutic preparation*. The commercial preparations, which follow the scientific ideas brought out in the last few

years, are divided into two groups, preparations of the *whole extract* of the ovary and preparations of *corpus luteum*. Because of what I said in Chapter II, I shall merely draw the conclusion here that extracts of the whole gland should always be used. While our knowledge remains as vague as it is, we shall have to resign ourselves to the empirical use of the total extract. If in certain patients there is a very intense genital symptomatology, the action of the whole extract may be reinforced by the addition of, or alternated with, extracts of the corpus luteum.

Of both these preparations, total as well as partial, I prefer those made from the *desiccated product*, compressed or in capsules, to the *glycerinated extracts* very common in the market. Some of the latter are evidently useful but in less degree and the effect lasts a shorter time. At present the hormonal content of the glycerinated extracts does not correspond to the total endocrine value of the gland. Guilera⁶ has proved that parts of the ovary which are histologically very important may be changed by their prolonged stay in glycerin, which confirms this suspicion. According to Schickele,⁷ the alcoholic extracts are very much more active, but, *a priori*, are subject to the same objection as the glycerinated; that is, they represent but a small part of the total hormone. Therefore I have not used them.

Mode of Administration and Dosage

In what way and in what doses should we administer ovarian preparations? Only exceptionally do I use subcutaneous injection, when it happens that the woman's digestive apparatus is disturbed, or in rare cases wherein intense ovarian therapy being indicated and administration by mouth is repeatedly a failure, I am forced to resort to subcutaneous injection before declaring the remedy useless. *Ordinarily, then, I recommend opotherapy by mouth.* It has the advantage of being convenient and permits repetition of the dose several times a day, thus stimulating the function of the languishing gland at short intervals. Besides, the digestive apparatus is apt to tolerate ovarian preparations very well.

⁶Guilera: Oral communication, 1918.

⁷Schickele: Op. cit., note (14), page 19.

The dose in which ovarian preparations should be employed varies widely according to the preparation, the clinical case, and the individual. Hence it appears to me childish to fix a general dose, as many writers do. Each patient requires her own dose. Even this is not constant, but varies in the different phases of her climacteric according to the importance of ovarian insufficiency in each stage. In general I may say, however, that the dose prescribed in books is insufficient. I believe in current practice ovarian therapy often fails because of the scantiness of the doses employed. Keep in mind the absolute harmlessness of these extracts if to intensify the treatment it is necessary to depart from the dose indicated for each preparation.

These doses may be continued for weeks if contrary indications are not deduced from clinical observation. The best time for their administration as with all opotherapeutic preparations, is after meals. In general, if the menses recur, it is proper to suspend the medication at least for the first days except in cases in which, on the contrary, the menstrual period constitutes an indication for the continuance and even an intensification of the treatment. This occurs, as we shall see presently, in certain metrorrhagias.

Results of Ovarian Therapy

The results of ovarian therapy in the climacteric are excellent, in general. Cases are really rare in which the symptoms are not improved, more or less, at the end of a short time. The menstrual disturbances, many of the circulatory symptoms (suffocation, tachycardia, hypertension, etc.), many of the nervous symptoms (pains, pruritus, etc.), the psychic disturbances, obesity itself, climacteric asthma, and so forth, are lessened almost without exception, when the treatment is correctly adjusted to the given case.⁸

A certain number of cases of pathologic menopause, on the other hand, resist ovarian medication. Of these failures a small

⁸I do not care to take up the recent statements of many physiologists as to the uselessness of ovarian therapy. The positive experience of clinicians is so overwhelming that these statements should be considered only as an example of how grievously one may err scientifically in the name of science.

group must be charged to intrinsic defects in the chosen preparation. Anyone making an extensive use of opotherapeutic remedies will note the great variability of the results obtained from different preparations. This variation obtains even with the same preparation if different brands are employed. Sometimes upon failure it is only necessary to discard the tablets employed and use others of the same preparation made by the same firm, whereupon therapeutic benefits previously lacking will be obtained. Another group of cases are failures, as I said before, because the doses are insufficient, the physician prescribing with excessive timidity. Finally, other failures must be ascribed to the symptoms which one is attempting to treat but which are somewhat remote effects of ovarian insufficiency and therefore are only remotely influenced by corresponding opotherapy. These are the symptoms produced by the other endocrine factors collaborating in the crisis and which intervene in greater proportion than the ovarian. Or rather, they are manifestations related to the previous pathologic state of the organ or system which presents the symptomatology. For example, climacteric obesity due to ovarian insufficiency and also the thyroid and perhaps hypophyseal disturbances noted further back, will not be influenced markedly and in a complete manner by simple ovarian therapy. In certain patients with cardiac or aortic disturbance, the suffocations and other circulatory changes of the menopause are apt to be especially intense, and also especially rebellious to ovarian medication alone. Thus I might multiply examples.

Other Opotherapies in the Climacteric. Thyroid and Antithyroid Therapy

Besides treatment with ovarian products various other glandular preparations have been advised in the crisis, those from the thyroid, the suprarenal, and so forth. It must be taken into account first of all, that in cases of premature menopause the amenorrhea may be the consequence of a hypophyseal or thyroid insufficiency and therefore, hypophyseal or thyroid therapy is

indicated, not ovarian, as an excitant of menstruation. Jona⁹ and others have brought this out.

Moreover, the impossibility of formulating indications from a general point of view can be deduced from a pathogenic study of the critical age. In each case various opotherapeutic remedies will be indicated. But in each case they will be different, since in different women the endocrine elements are never the same. *The indications, therefore, will depend on a careful study of the endocrine symptomatology which the patient presents.*

As far as the thyroid is concerned, as I said on page 46, because of the frequency with which hyperthyroid reactions predominate in the crisis, thyroid therapy is rather contraindicated, for these reactions may be exacerbated under thyroid treatment. After careful examination of cases with respect to the functional state of the thyroid, I divide them into three groups:

1. The most numerous group is composed of menopausal women with a predominance of the hyperthyroid symptomatology, tachycardia, palpitations, suffocation, and very lively vasomotor reactions, sweating, tendency to thinness, poor emotional control, motor uneasiness and general nervousness. In these thyroid therapy is contraindicated even in small doses. On the other hand antithyroid treatment is indicated.¹⁰

2. In another also very numerous group there are presented the somewhat equivocal symptoms of thyroid instability, that is, a mixture of hyper- and hypofunctional manifestations of difficult delimitation. In these cases the problem is more complicated. Small doses of thyroid extract may be useful, but on condition that they be very small and the patient be closely watched, in order to suspend the treatment at the slightest indication of re-erudescence of hyperthyroid manifestations. As a means of picking out these cases and watching the treatment the following rule may serve. Thyroid may be given only when the basal metabolism is lower than +20. If no means are available for making

⁹Jona: *Gaz. degli Ospedali*, 1916, page 420. This was the case of a woman prematurely menopausal. Ovarian preparations had been useless. But the case was really one of Fröhlich's disease (hypophyseal insufficiency) and consequently hypophyseal therapy caused the menses to reappear after an amenorrhea lasting twelve years.

¹⁰In my study on the treatment of hyperthyroidism, note (9), page 269, I indicated the details of this treatment; physical and psychic repose, proper diet, ovarian extract, belladonna and perhaps antithyroid serum.

this test, then a cruder but useful rule is that the patient be not thin nor have a permanent tachycardia above 100.

3. In the third group come those with hypothyroid symptoms, edematous obesity, dryness of the skin, falling hair, great sensitiveness to cold or affections of the skin and joints. Here we shall employ full thyroid therapy in doses which progressively increase until we reach the amount which obtains the maximum result without provoking hyperthyroid reaction. This amount can only be determined by observation of the case. The rules given above will also serve here: that the basal metabolism not exceed +20, or lacking this test, that the patient not lose weight excessively nor have a permanent tachycardia above 100. Here let me recall that fear of such medication is in general without foundation. This fear, common among the laity and even among many physicians because of the alleged recurrence of grave symptoms, constitutes a serious hindrance to its use. Such accidents are becoming rarer and cases of serious damage through thyroid medication are exceptional, less numerous than those due to any other therapeutic proceeding. And the minor symptoms which we recognize as therapeutic thyroidism, nervousness, insomnia, tachycardia, digestive disturbances and thinness, in short, an artificial and reduced reproduction of spontaneous hyperthyroidism, are easily avoidable when the medication is managed with some care. When these symptoms do appear, they almost always yield easily to simple suspension of the treatment.

Indications for Suprarenal Therapy

With respect to suprarenal medication it strikes me as baseless to recommend this treatment a priori in the menopause, as Martin does according to Schickele. On the contrary, we know that in the immense majority of cases suprarenal phenomena of hyperfunctional type predominate. Hence such medication would be contraindicated, since it would increase the hypertension and the other phenomena accompanying it. As we possess no remedy which restrains heightened suprarenal activity, we must content ourselves in these cases by resorting to symptomatic remedies. That is to say, arterial tension must be lowered through drugs.

I shall speak of these presently. Cottenot¹¹ praises roentgenotherapy over the suprarenal region as a modifier of the hyperfunction of these glands. But this is a means little used. I have seen it attempted on occasion without result. Cool baths have also been recommended.

Thus suprarenal therapy is limited to some rare cases with such symptoms as hypotension, asthenia, and pigmentation. These are the signs of a more or less intense suprarenal insufficiency which almost always has been present long before the crisis.

Hypophyseal Therapy and Other Glandular Medication

The intervention of the hypophysis as I have said, is apt to be secondary in the critical age. Therefore, hypophyseal medication has a relative importance in this age. As we know, its action is apt to be revealed almost without exception by hypofunctional symptoms, the most striking being abdominal adiposity. As the hypopituitary syndrome appears to be clear, we have an indication for hypophyseal therapy in cases of early amenorrhea, with rapid increase in weight and localization of fat chiefly in the abdominal region.

Other glandular extracts, such as the mammary, parathyroid, biliary, pancreatic (insulin) and so forth have their indications in the menopause, but these are of a symptomatic order. Hence I no more than mention them here.

General Diet in the Climacteric. Criticism of Severe Diets

As a general dietetic rule, in the menopause without important complications I insist on the great value of keeping to a diet which is little toxic, predominantly vegetarian and not very abundant. A strictly temperate habit in taking food is even more necessary than qualitative precautions as to this kind or that. Women in this age should eat no sausage, preserves, heavy meats, such as pork and game, and no toxic or stimulating foods. At noon there is no harm in eating white or red meat, all kinds

¹¹Cottenot: *Action de rayons X sur les glandes surrenales* These de Paris, 1913.

of fish, broths and so forth. At night the food should be especially scanty, limited to a small portion of white fish, fowl or croquettes, and green vegetables and fruit. These should be omitted from the principal meal.

Most important are beverages. Climacteric women should drink no alcohol of any kind. They may drink water moderately, at least with meals. They should avoid charged waters, even those not alcoholic, as these favor the flatulence so frequent in this age.

In general I do not approve of those diets imposed by physicians which are a nightmare to the patient, especially where the condition is not serious or of long duration, as in the climacteric. We must admit that our ideas are very poorly defined as to the mischief of certain groups of foods which are subject to scientific prejudice and excessively dependent on laboratory tests inapplicable in practice. For this reason and because of the complaints coming from almost every one on being subjected for months and months to an excessively rigorous régime, I feel such to be a pedantic abuse of scientific authority on the part of the physician. This is particularly true when he gives his orders in excessive detail, fixing to the smallest point the quality and quantity of food to be taken. There are very few patients who can reasonably be said to be going too far when they eat meat of this or that kind or some other food. But within this tolerant criterion I believe the above advice will be useful to women however slight the climacteric symptoms. In general the middle and upper classes of society eat excessively after the thirty or thirty-fifth year. Hence it is well to spread the idea among men and women that they should limit their rations, especially all nitrogenous foods and particularly at night, to an amount which would supply a minimum amount of waste for the organism and provide at the same time improved digestive powers. Aside from these general indications the alimentary regimen of menopausal women will have special peculiarities in certain conditions such as diabetes, obesity or gout as I shall indicate presently.

Exercise, Walking, Recreations, Travel, Motoring

Systematic exercise is very important in the general hygiene of the critical age. In the great majority of cases the woman is

apt to lead a sedentary life which favors to the highest degree the appearance of such disturbances as the circulatory, metabolic, and nervous symptoms which now begin. In Spain and especially in the villages and small towns this sedentariness is so constant and marked that it surely takes part in a given percentage of certain climacteric complications. For example, obesity is much more common in Spain than in other countries where woman has greater social activity.

The exercise of choice is walking. A walk should be taken twice a day, before and after the noon meal, but violent recreations, I believe, are contraindicated. It is an error to put a strain on the circulatory system in this age. Golf may be excepted from this general consideration. I have noticed in many women the benefits of practicing daily this mild exercise which aids the circulation, and prevents putting on weight. Moreover it breaks the spiritual monotony of life inevitable when the mind is exclusively dependent on the petty problems of the home to which so many of our women are tied. For the same reasons travel is useful. Kisch¹² advised against too much railroad travel, but no one pays attention to this nowadays, and rightly. Vinay¹³ stresses the advantage of motoring because of its exciting influence upon general nutrition which Mouneyrat has proved.¹⁴ As he has observed, the automobile also has an advantage in causing an inhibition of mental processes through the intense expectation produced by velocity upon the senses. Thus in the automobile the preoccupied mind is given rest and in the best way. I have often called attention to this fact which is of indubitable therapeutic utility.

Massage, Electrotherapy, Hydrotherapy

Massage is of considerable value in climacteric women with many circulatory disturbances or with marked tendency to obesity. But for financial reasons this must be an exceptional means. Hence in practice I limit its indication to certain special cases, for example, to localized adiposity, as we shall see.

¹²Kisch: *Op. cit.*, note (13), page 19.

¹³Vinay: *Op. cit.*, note (12), page 19.

¹⁴Mouneyrat: *Influence de l'automobil sur la nutrition general.* *Compt. Rend. de l'Acad. des Sciences*, 1907.

The various proceedings, electrotherapeutic, or roentgenotherapy have times of special application, which will be indicated later.

Hydrotherapy in ordinary cases should be limited to the usual bath, taken cool. Many women have the habit of taking baths excessively hot, an undoubtedly harmful practice at this age, as I have shown.



Fig. 18.

Sexual Relations, Amusements, Occupations

The classic works on the menopause say that when this age begins it is proper to break off sexual relations. In the adjoining cut taken from Gardanne's book,¹⁵ which I could not resist the temptation of reproducing, there is expressed in delightful

¹⁵See note (70), page 168

allegory the point of view held by physicians of that period on this particular point. A protecting shield guards the matron who is still beautiful from the arrows of love, while medicine offers to comfort her with advice and remedies. Needless to say this classic advice is of little efficacy, since the recommendation of abstinence either corresponds with the woman's spontaneous decision, in which case it is unnecessary, or it is contrary to the sexual instinct, which is still alive or heightened, in which case we may be certain that the physician's advice will not be heeded. Vinay in discussing this point recalls one of Tilt's tables which showed that in England every year from 3,000 to 3,500 women are married who are between 45 and 55 years of age. Of these women, and the many others of the same age not included in these statistics which relate solely to legal marriages, how many would cling to single life to follow advice which, while hygienic, is of very doubtful value?

Keeping in mind the large part played by psychic factors in the etiology of climacteric symptoms I advise, even insist upon, all possible distractions and occupations which clarify the spiritual atmosphere in which she lives if that atmosphere is not conducive to peace. For unfortunately neither the Spanish woman's education nor our customs, outside the large cities, afford many means of improving the psychic conditions which are always difficult to vary in this epoch of life. This is because the character is now definitely formed and adapted to its intimate and social environment. But simple occupation is really useful here. From Ovid's time, work, occupation, is the supreme remedy for every episode in sexual life.

CHAPTER XXVII

TREATMENT OF CLIMACTERIC SYMPTOMS AND INCIDENTS

(B) ALLEVIATION OF SYMPTOMS

Treatment of the Menstrual Disturbances. Hemorrhage

In the preceding chapter I explained the general rules of diet and hygiene applicable in the majority of cases and the fundamental treatment of the climacteric symptoms and incidents; that is, ovarian therapy, alone or associated with the other opotherapeutic resources which endocrine study may suggest in each case. But, besides these general remedies each class of climacteric symptoms presupposes a special treatment which we shall consider for each case.

The menstrual disturbances require scarcely more than ovarian treatment. When the fluctuations of the withdrawal occur in a progressive descent or with irregularities which are not very great, we shall use simply whole ovarian extract which will regulate the upset in so far as is possible.

Metrorrhagia requires in the first place a very careful local examination. If the bleeding depends on uterine lesions, inflammations or tumors, benign or malignant, the case passes to the jurisdiction of the gynecologist. He will make use of the classic and recent therapeutic remedies, x-ray, radium, electrotherapy or surgical intervention which are outside the field of the internist.

In case the gynecologist is certain of the integrity of the patient's genital tract, we must seek the cause of the hemorrhages in conditions which are properly endogenous, that is, endocrinal. On pages 30 and 121 I explained that my present experience is unfavorable to the hypothesis that uterine hemorrhage results from insufficiency of certain hormones, as of leuteolipoid origin. Neither by employing the lutein preparations in large doses, nor

the preparations especially made with these inhibitory hormones (*sistomensina*, etc.), have I obtained lasting effects. In cases like those which I cited in the first edition of this book in which suppression of the hemorrhage was achieved, this result was temporary, the bleeding almost always recurred, notwithstanding persistency of treatment, thus giving me the impression, when the menstrual cessation was definite that it was due rather to spontaneous evolution of the process.

I do not deny, however, that in these cases of hemorrhage without lesion, a certain mild ovarian therapy, steadying the unstable function of the gland, may be useful. But I believe that whole ovarian substance is superior to the corpus luteum alone. At any rate, our procedure in these cases should be oriented in this way: 1. Subject the patient to rest and institute general care of the uterine hemorrhages. 2. Administer the usual classic remedies proper to these cases, such as ergot, hydrastis, hamamelis, etc. 3. Add, as a regulator of the ovarian function, a discrete dose of ovarian extract. 4. Examine the endocrine and general conditions of the patient, in case other elements are found which may influence the hemorrhage. As said in Chapter XI these conditions are principally thyroid insufficiency and arterial hypertension.

With regard to the thyroid upset, it is indeed evident that at times we find in these women symptoms of thyroid insufficiency more or less marked. Levy and Rothschild,¹ Recasens,² and others have described cases of this kind. I have described similar cases, especially one of a climacteric woman suffering from severe hemorrhages and free from pelvic disease. A diagnosis of thyroid insufficiency here was based upon chilly sensations and a suspicious increase of weight. Cure was effected with the proper opotherapy and the hemorrhages ceased at the same time. Izquierdo³ has published a case of great demonstrative value although in a young woman. Again, the hemorrhages may coin-

¹Levy and Rothschild: *La petite insuffisance thyroïdienne et son traitement*. Paris, 1913. In their volume the writers give a résumé of the literature on this and other points of contact between thyroid lesions and the genital functions in woman which may be read with great benefit.

²Recasens: *Op. cit.*, note (1), page 101.

³Izquierdo: *Op. cit.*, note (18), page 124.

cide with hyperthyroid states as I have said and Botín⁴ has confirmed. It is a paradoxical phenomenon but indubitable that contrary thyroid states may give rise to the same symptom.

Therefore in those cases, which are by no means rare, wherein a hypothyroid symptomatology exists characterized by obesity, fugitive edemas, somnolence, chills, apathy, low basal metabolism, etc., we should employ thyroid therapy alone or combined with hemostatic remedies and perhaps ovarian substance. If, on the contrary, there is hyperthyroidism, we should rely on the antithyroid resources already enumerated. And in either case, we should employ calcium salts, in virtue of the theoretic considerations explained on page 124 and which practice fully sanctions.

With regard to hypertension, if its existence is confirmed, it is evident that the employment of the hypotensive remedies which I shall explain later, will contribute in quieting the hemorrhagic tendency.

Let me add that mammary extracts by mouth or injection have an inhibitory action whatever the mechanism of the uterine hemorrhage. The action is uneven but at times immediate. Therefore the physician should hold these in reserve for such conditions.

Vicarious Leucorrhea and Hemorrhages

In leucorrhea which we may call vicarious, that is to say, where there is no indication of grave lesions of the genital organs, local treatment such as astringent irrigations should always be accompanied by ovarian, and perhaps thyroid therapy, when there are symptoms of insufficiency of the latter gland (Levy and Rothschild⁵).

The treatment of vicarious hemorrhages should be based on the pathogenic data already explained, that is, upon the association of these three therapeutic elements: 1. Combat ovarian insufficiency in general as the occasional factor of the disturbance with ovarian extract. 2. Combat the hypertension if, as is the

⁴Botín: *Commentarios clinicos al tratamiento opoterapico en ginecologia y obstetricia* Rev. Espanola de Obstetrica y Ginecologia, April, 1918.

⁵Levy and Rothschild: *Op. cit.*, note (1), page 391.

rule, it exists by the methods I shall presently describe. 3. Treat such local lesions, apparent or hidden, which play the rôle of *locus minoris resistentiae*: chiefly gastric ulcer, hemorrhoids, pulmonary lesion, etc.

I say nothing of the treatment of uterine processes, inflammatory and neoplastic, nor of mammary tumors and inflammations, since it concerns the gynecologist or the general surgeon, leaving to the internist only the matter of early diagnosis.

Treatment of Hypertension

In the circulatory symptomatology of the critical age hypertension is a fundamental manifestation which therefore requires primary therapeutic attention. If we can relieve a menopausal woman of hypertension, it is certain that we shall relieve her of many complaints, and we shall deliver her from several of the dangers which imperil her. The treatment of climacteric hypertension includes several points:

1. **Opothérapie.**—The ovarian extracts, total or partial have, a positive hypotensive effect as many writers have demonstrated.⁶ Therefore the existence of hypertension is an indication for intensifying ovarian therapy. Nevertheless, I should state my impression that the clinical results do not correspond, in this respect, with the experimental results; the good effects which are achieved must be ascribed rather to the treatment as a whole than to a specific action of the glandular substance.

2. **Hypotensive Remedies.**—It is well to supplement hypotensive medication by means of auxiliary remedies. The preparations of iodine, especially in its different commercial organic forms, are manifestly useful, employed in repeated doses several times a day, not excessive in their full amount nor long con-

⁶For a résumé of the question as to the effects of ovarian extracts on arterial pressure see:

(a) Biedl: Op. cit., note (15), page 19.

(b) Pende: Op. cit., note (17), page 19.

(c) Villemain: Op. cit., note (11), page 19.

(d) Carnot: Op. cit., note (18), page 338.

(e) Jauregg and Bayer: Lehrbuch der Organotherapie. Leipzig, 1914.

(f) Swale Vincent: Internal secretion and the ductless glands. London, 1912, and op. cit., note (36), page 149.

(g) Livon: Sur l'action des extraits du corps jaune de l'ovaire. C. R. de la Soc. de Biol., 1909.

tinued. The existence of hyperthyroid symptoms must be sought as an important contraindication. When these are manifest, as occurs, for example, in patients with simple goiter who tend to become hyperthyroid on reaching the critical age, iodine should be prohibited absolutely. In my judgment, the mere existence of a simple goiter is quite enough, in even the absence of hyperthyroid symptoms, to contraindicate iodine in the menopause. I have very often seen such cases brought to the point of iodine basedowism, perhaps difficult to overcome.⁷ With the exception of these cases, in the hypertonic climacteric iodine produces effects frankly beneficial upon all the symptoms derived from hypertension. It is one of the most useful remedies in this period of life.

Preparations of *viscum album* (European mistletoe), sodium nitrate and benzol benzoate being free from the dangers associated with iodine compounds, are to be recommended. I have used them a great deal, either alone or, more frequently, alternating them with iodine compounds.

3. Regulation of Diet.—As in all the hypertensive states, it is impossible to put aside regulation of the diet. In the mild ordinary cases, the restrictions and generic modifications explained under general treatment are sufficient.

In more marked cases I am accustomed to put the patient on one day of milk diet, in every fifteen or twenty days, not allowing more than a liter and a half of milk in the twenty-four hours. Even a day of fasting is advantageous. This is complete or partial, a light vegetable broth being permitted. Do not forget that these women are apt to be hypercholesterinemic and, therefore, eggs and other foods rich in cholestérine, usually recommended in this kind of dietetic treatment, should be restricted. Rarely does climacteric hypertension require stricter dieting.

4. Exercise.—It is indispensable that these women so little inclined to exercise be required to without carrying it too far. In many of my cases this means has brought good results in hypertension and its consequences.

⁷See Bonilla: *Tratamiento médico del hipertiroidismo*. *Siglo Médico*, 1919.

Treatment of Vasomotor Phenomena: Opothrapy; Belladonna, Hypotensive Remedies, Diet

The vasomotor phenomena, the suffocations, typical of the climacteric demand as treatment, in the first place, whole ovarian extract. In many cases it improves these disturbances, always provided that the remedy be used in sufficient doses. I have often seen women greatly harrassed by this symptom who had taken ovarian extract and considered it a failure. Simply by doubling or further increasing the dose of the same preparation they had been taking they were rapidly improved. Nevertheless, ovarian extract, of itself, is not enough except in very mild cases. It is necessary to associate with it the general remedies, already discussed, which lessen the circulatory and nervous plethora characteristic of the climacteric.

In this direction belladonna is most useful as a regulator of the autonomic vegetative system. This is one of the great therapeutic means of combating the vasomotor symptoms of the climacteric, by virtue of the physiologic reasons explained in Chapter V. Belladonna should be employed in sufficient doses. In general it is a remedy which physicians handle with excessive timidity. In these cases of intensive vasomotor reaction, I prescribe 30, 40, or more drops a day, divided into doses of 10 to 15 drops of the tincture, in association with ovarian extract or antithyroid serum. Previous examination of the patient's resistance is made, since it is known that each individual has a peculiar susceptibility to belladonna. This is particularly true of the hyperthyroid condition so frequent in menopausal women who are peculiarly responsive to it.

When the suffocations are severe and coincide with a permanent hypertension, a condition not always occurring as contended by some writers, the hypotensive remedies before mentioned should be used.

Regulation of diet is also indispensable, either as a mildly anti-toxic regimen, as indicated in the previous chapter, or with the vigor described in the treatment of hypertension. But in either case the physician must insist on the necessity of the patient's refraining from every kind of alcoholic drink. I have often seen the favorable influence of this one omission alone upon suffoca-

tion and have frequently dwelt upon this point to which Jung⁸ also gives a just importance. Naturally the same thing may be said (although in lesser degree) of other stimulating foods and drinks, such as coffee and tea. These beverages may be replaced by malt according to Jung, or their use may be merely restricted. I have also noted a favorable influence obtained by forbidding tobacco to those climacteric women who smoke a great deal. This is rarely required of Spanish women, for the majority of those who smoke do so only while young and then but moderately. In my opinion they smoke in response to environmental reasons, because it is the fashion. Perhaps the act is not free from a sexual feeling which I may not explain here.

Yet I should say that there is an occasional case wherein the suffocation resists all these treatments, however rigorous, careful and prolonged they may be. Such a one will persist in spite of every effort, especially in women with artificial menopause, surgical or roentgenologic.

Treatment of Simple and Paroxysmal Tachycardia

Simple tachycardia is benefited by a general antiplethoric treatment consisting of ovarian extract, diet, and hygiene rather than by antithyroid remedies, when there are symptoms which permit one to suspect a hyperthyroid element in the background.

Paroxysmal tachycardia, of more complicated pathogeny, also requires more complicated treatment. Therapeutic measures here will comprise the following: (1) Ovarian therapy in energetic and continued doses, and at times antithyroid or thyroid treatment, perhaps with the addition of suprarenal extract in small doses, depending on the endocrine reactions which examination of the patient reveals. (2) The dietary regimen, which should be watched closely from two points of view; the general antitoxic and the properly digestive. It is known, indeed, that many women with accessional tachycardia suffer various digestive disturbances, particularly flatulent dyspepsia which I described in Chapter XIX. These act as "occasional cause," the appearance of the attack coinciding with the periods of impaired

⁸Jung: *Die Behandlung der klimakterischen Beschwerden des Weibes*, Deutsch. med. Wchnschr., 1912.

digestion. (3) Circulatory medication properly speaking. I have already indicated that the phenomena of subjective palpitation and of paroxysmal tachycardia in menopausal women when they are very intense and repeated, should make one suspect a myocardial change, perhaps very slight, but in no wise to be ignored. In these cases it is a mistake to apply cardiac tonics, which sooner or later may excite and uselessly weary the heart. Therefore the regimen should be limited fundamentally to opotherapeutic and dietetic measures, making use of tonics only when these are really indicated, as in case of hyposystole and always with prudence, as in the use of spartein, strophanthus and its derivatives, squills and digitalis. The treatment of the attack is very limited in its resources. Bromide of camphor, two or three doses of 10 cgm., is useful in not very violent attacks. In more severe cases recourse may be had to injections of morphine with atropin. In some cases the injection of apomorphin has given good results. If the attack continues for a long time it will be advisable to strengthen the heart with caffeine or camphorated oil, since not rarely at the end of an hour some symptoms of insufficiency of the myocardium may appear.

In all these given circulatory conditions of hypertonic predominance carbonated baths are very useful. These may easily be prepared at home, either with the commercial products which are sold for the purpose (Nauheim, Royat salts, etc.) or simply by dissolving in the bath two kilos of sodium bicarbonate and adding slowly, after the introduction of the patient, a liter of hydrochloric acid diluted in another liter of water, being careful not to spatter the skin. The temperature should not be high, an average of 32° C. The patient should be very quiet during the bath, the duration of which is ten or fifteen minutes. Dry by light pressure without friction. Rest in bed at least an hour. Number of baths, two or three a week.

Utility of the Ovarian Preparations in the States of Mild Cardiac Insufficiency in the Climacteric

In conditions of cardiac insufficiency, subacute and acute, which I described in Chapter XII, the opotherapeutic treatment takes second place, that is from the pathogenic point of view.

But practically its usefulness is worthy of notice in the treatment of the circulatory symptoms occurring in the critical age, the possible influence of which in the production of symptoms should always be kept in mind. One should then add whole ovarian extract in vigorous doses to the principal treatment, digitalis, milk diet, etc.

Angina Pectoris

The symptoms of anginal type, relatively frequent in the climacteric age, which appear alone or linked to phenomena consequent to cardiac insufficiency, are also happily influenced by ovarian therapy associated with the proper dietetic management. Geissler⁹ pointed this out and I have confirmed it many times. Generally it concerns hypertensive women, perhaps arteriosclerotic, thin or more frequently obese, in whom rigorous reducing treatment is indispensable. I shall refer to this again.

Symptoms of the Nervous System. Pain

Among the symptoms of the nervous system there is a group which, to judge by the therapeutic benefit obtained from the use of ovarian preparations, appear to depend directly on ovarian insufficiency. These are the neuralgic pains, localized variously, but chiefly bone and muscular pains, vague, shifting but persistent, which frequently torment menopausal women. The presence of these symptoms is, then, a precise indication for instituting a vigorous ovarian treatment. Of course this is not incompatible with the prudent use of the usual analgesics, aspirin, phenacetin and their like, the use of which many menopausal women so abuse.

The frequent hypertensive headaches require the employment of the hypotensive remedies previously explained. There are, however, rebellious cases, resistant to all remedies which only cease when the attack spontaneously diminishes and with it the hypertension. Indurative headache is apt to yield to massage and to applications of heat to the nape of the neck, applied by means of compresses wrung out of hot water and placed a

⁹Geissler: *L'opotherapie ovarienne contre l'angine de la menopause*. Sem. Med., 1900, lxxxvi.

little distance from the hair line but not directly on it. I also make use of the following technic: apply to the neck, below the hair line, wet compresses and blow over them until complete evaporation a jet of hot air from an electric drier. But besides these remedies advised by Edinger, my experience has revealed the promptness with which ovarian therapy and perhaps thyroid in small doses act in such conditions.

Asthenia

The asthenia of climacteric women should be treated by suprarrenal therapy if the arterial tension is normal or low. Small doses of strychnine also exercise a useful part, perhaps by their exciting action on the adrenalin secretion. When the characteristic weakness of asthenia coincides with hypotension the hypotensive remedies already described are used. It is rare that this symptom is present alone. It almost always appears together with other climacteric symptoms, principally nervous and psychic, of the neurasthenic type. In any case, ovarian treatment is of indubitable usefulness.

Pruritus

Pruritus, general or localized, as I have said, is often due to latent diabetic states, not revealed by spontaneous glycosuria but rather by hyperglycemia. Therefore, when it comes to this state of affairs ovarian extract and an antidiabetic diet should be prescribed. These will likely be sufficient to cause cessation of the pruritic distress. Cases of vulval pruritus dependent upon kraurosis and senile lesions of this region, I have already indicated respond perfectly to ovarian opotherapy as shown by Schickele and Graves. It is clear that topical applications may be associated with this treatment.

Dizziness

Cases of dizziness require careful study and treatment according to the change producing it. If hypertension is the factor a hypotensive regimen is indicated; if due to vasomotor irritability then an antitoxic regimen with belladonna. When arteriosclero-

sis is present, the regimen must be hypotensive; digestive disturbances require diet and remedies which we shall explain presently; on the other hand auricular disturbances of the Meniere type respond to diet, quinine, etc. In every case ovarian extract should be given in addition.

Insomnia and Somnolence

Insomnia, a symptom so common and stubborn in some of these women can be combated with proper diet with emphasis on antithyroid remedies, especially diet, antithyroid serum, belladonna, and ice to the neck on retiring, according to the clinical indications. It is precisely in such cases one should exhaust all remedies before turning to the ordinary hypnotics such as veronal. These are only too soon abused.

States of somnolence, which are much rarer, should be carefully studied with respect to the nervous system if there is hysteria; to the urinary system if uremic; to a general metabolic breakdown, like diabetes, and to the endocrine system for evidences of hypothyroidism or hypopituitarism. The diagnosis of any one of these conditions carries with it the corresponding treatment.

Psychic Disturbances

The psychic disturbances of the menopause require chiefly ovarian therapy, as do all the other climacteric symptoms. But perhaps the psychic symptoms stand in the front rank as indications for ovarian extract. Many writers have discoursed at length upon the efficacy of glandular medication in these cases. I call attention especially to the thesis of Alaize,¹⁰ for its discussion of opotherapy; to Jauregg and Bayer¹¹ and to Carnot¹²; and also to the opinions concerning the influence of the internal secretions in mental pathology previously referred to on page 196. In addition I desire to cite the work of Strecker and Keyes¹³ and of P. Marie. Naturally, the psychic disturbances directly linked to the climacteric are especially benefited by this medica-

¹⁰Alaize: *Op. cit.*, note (8), page 19.

¹¹Jauregg and Bayer: *op. cit.*, (6, e), page 393.

¹²Carnot: *Op. cit.*, note (18), page 338.

¹³Strecker and Keyes: *New York Med. Jour. and Med. Rec.*, July, 1922.

tion. Such disturbances are emotional instability and certain perturbed sexual reactions. Others are found among the psychopathies properly speaking, especially the lighter forms not linked to profound states of nervous predisposition such as paranoia and melancholia. The third group of psychic disturbances includes the neuroses, certain forms of hysteria closely related to the sexual episode and cases which have been regarded as neurasthenia. P. Marie¹⁴ insists that the efficacy of ovarian extract is increased the earlier it is employed. Burnam¹⁵ and Kelly¹⁶ claim that ovarian therapy is especially valuable in that group of cases which the Americans designate by the phrase "run-down conditions." By this is meant states of physical and psychic exhaustion linked to ovarian insufficiency and generally diagnosed as "neurasthenia." This condition is characterized chiefly by intense fatigue following any mental or physical work, particularly during menstruation, although the most careful examination discloses no important lesion of any organ or apparatus. Here large doses must be prescribed in order to obtain appreciable results.

In cases, which we know are frequent, wherein the psychoses are associated with marked hyperthyroid reactions, it will be useful to combine ovarian therapy with antithyroid treatment. On the other hand, when symptoms of depression dominate to the extent of psychic and physical apathy, it is well to associate ovarian therapy with small doses of thyroid, and if there is hypotension with suprarenal or pituitary extract.

Pharmacologic and Physiologic Treatment of the Psychic Symptoms of the Climacteric

The pharmacologic treatment is the usual one in these affections. Belladonna and opium preparations are especially indicated in cases with excitation. Sometimes the tincture is better in doses of 10 to 15 drops given once or twice a day, accord-

¹⁴P. Marie: *Au sujet des troubles mentaux de la ménopause*, Soc. de Therap., March, 1921.

¹⁵Burnam: *Corpus Luteum Extract in Gynecologic Practice*, Jour. Am. Med. Assn., 1912, lix.

¹⁶H. A. Kelly: *Medical Gynecology*, Phila., 1908.

ing to the severity of the case. Schickele¹⁷ advocates calcium salts for these women as regulators of the general nervous excitation in preference to all other sedatives. I almost always use calcium lactate, three to four grams daily.

The physiologic methods employed in very intense cases are isolation, rest, hydrotherapy in its various forms, and require no further comment.

Psychotherapy and the Menopause

In regard to psychotherapeutic treatment, its importance has been emphasized by Walthard¹⁸ especially in cases of disturbances of the sexual feeling. Indeed there are women who are so benefited by this means that they return to a normal condition. In others, the direct disturbance of libido supercedes everything. When this feeling has been so strong that it has torn the woman from her usual habits, from her old and legitimate affections, perhaps from the precepts of her moral background or of her religion, psychotherapeutic attempts will be less efficacious but should always be attempted. In general, it is evident that the moral and religious convictions of the individual and of the atmosphere in which she lives, and especially her degree of psychic and sentimental culture act very much on the determination and intensity of this kind of symptom and can, therefore, be made use of in her treatment.

Treatment of Climacteric Obesity

A most important chapter in the therapeutics of the menopause is the treatment of obesity whose stubbornness is, at times, so great at this age that, as I have said, it constitutes one of the peculiar clinical characteristics.

I cannot sufficiently stress the value of combating the obesity with energy and from its beginning. The advice of the hygienists, so often pedantic and useless, should receive our strongest support on this point. It is evident that in obesity the vital

¹⁷Schickele: Op. cit., note (14), page 19.

¹⁸Walthard: (a) *Psyconeurose und Gynäkologie*, Monatschr. f. Geburtsh. u. Gynäk., 1911, xxxvi.

(b) *Ueber die Bedeutung psychoneurotischer Symptome für die Gynäkologie*. Zentralbl. für Gynäk., 1912.

abilities are lessened in direct proportion to the patient's age. Climacteric obesity, then, should be combated at all costs. This is a matter of principle since obesity is as hard to treat as it is easy to prevent. Fortunately, the esthetic criterion imposed by the present fashion, which shows no indication of dying out, assists the task of the physician who has been accustomed to struggle with an antagonist greater than the obesity, the fat person herself. It is indubitable that the fashion for the slender figure has caused disturbances, illness at times disastrous. But all these are less harmful than the conditions produced by the fat itself. Hence I am not opposed to this vogue which sacrifices unduly the traditional esthetic elements on the altars of health. The woman who reduces may lose freshness and rounded contour and often the appearance of youth, but she will gain a greater agility and sprightliness and will postpone cumbersome old age. She sacrifices the esthetic or sculptural elements of beauty, which are essentially those of youth, in exchange for the dynamic element which is called "line," an element without sex and without age. It may be said, if I am permitted a paradox, that this woman who reduces purchases a prolonged maturity in exchange for a premature old age. In my judgment she makes a good bargain.¹⁹

The correct application of the reducing treatment presupposes, in the first place, a detailed clinical examination to determine how important the exogenous and endogenous factors have been in the production of the increased weight. Generally we find that it is due to the collaboration of both, overeating and sedentary habits on the one side and on the other metabolic disturbance dependent on ovarian insufficiency with or without hypophyseal and thyroid dysfunction. In consequence, the treatment must include all the elements of diet, physical exercise and corresponding opotherapy.

The alimentary regimen may be very severe. While in youthful obesity dietary restrictions are, on occasion, dangerous because they give rise to digestive and general disturbances, in maturity the obese organism is apt to tolerate well and even

¹⁹Of the recent writers who have expressed this same opinion, see the admirable pamphlet by Lucinani and Baglioni, *L'alimentazione umana secondo le piu recenti indagini fisiologiche*. Rome, 1917.

thrive under the imposition of a most rigorously restrictive diet. Ordinarily the individuals of a certain social status eat much more than they should. After the thirty-fifth year they go on eating as much as they did in youth, without considering that the organism in this age has reached a state of metabolic equilibrium in which small intakes suffice to keep up the total daily wear of the body. For this reason the climacteric or preclimacteric patient observes with surprise that with a third of her usual ration not only is she not debilitated on losing weight, as was anticipated, but feels just as strong and at the same time is relieved of many complaints. The details of the regimen cannot be given in a general way, since each patient requires her special restrictions according to the type of her previous nutrition, her circulatory and renal state, etc.²⁰ But as an outline to be modified in each case according to these individual peculiarities I may offer the following example. This will be well tolerated and furnishes from 1300 to 1600 calories according to the vigor with which it is applied.

First breakfast: A large glass of milk (200 or 250 grams) alone or with a little tea or coffee with no sugar or a small spoonful (6 grams); no bread or two slices of toast (about 20 grams).

Breakfast (noon): Two eggs, soft-boiled, as an omelet or poached. A main dish of one of the following: white fish (150 grams), ham (80 to 100 grams), veal, beef or chicken, roasted or fried, without sauce (80 to 100 grams). Green vegetables (150 to 300 grams) preferably beets, spinach or green beans, cooked with a little fat, or in a salad with oil and vinegar. For dessert, 150 to 300 grams of fruit in season, four or five plums, fifteen cherries or a large pear. A small French roll, 50 grams if entire, 25 grams if the crust only. A medium-sized glass of water. A cup of tea with lemon juice.

Luncheon: A glass of milk (200 to 250 grams) alone or with coffee; no bread or one or two slices of toast.

Dinner: An egg, a portion of fish, meat or chicken, as at noon; twice a week this may be replaced by 150 grams of puree of

²⁰See especially the recent monograph by M. Labbé, cited; note (4), page 239.

potato, lentils or peas; 150 grams of green vegetables. Fruit, bread and water, as at the second breakfast.

This outline can be adjusted to the requirements of each case. There are women with grave complications related to obesity such as angina pectoris in whom the whole restriction may be lightened at times in amounts equal to 800 or 900 calories. The more severe restrictions as to quantity may be lightened when necessary, as, for example, the absolute prohibition of carbohydrates, fats, etc. The absolute deprivation of liquids which some recommend and which many women spontaneously put into practice on the advice of friends should be reserved for exceptional cases. The slightest deficiency in renal function or a marked tendency toward phenomena of arthritic type contraindicate this treatment. And, in every case, as Labbé insists, the value of restricting liquids is only transitory. In accordance with this opinion I am accustomed to order every ten or fifteen days one or two days of restricted liquids, but not daily.

Physical exercise is an indispensable element in the treatment of climacteric obesity. A case of increasing weight at this age in which excessive sedentary life has not played the largest part is rare, especially in the women of our southern countries. And in practice, the physician must always contend against extraordinary difficulties in order to combat it. I have seen many women whose obesity was so grievous that it had finally induced them to seek treatment, having decided to make every sacrifice, yet they began their consultation by begging that "they be not obliged to take exercise." Faithfulness in submitting to this feature of the treatment even more than in accepting the dietetic restrictions is apt to weaken in these obese women, no longer young and to whom reducing has lost the esthetic value of earlier years. Only when this worry persists into the climacteric age, and in some cases it may not only persist but reach pathologic intensity, or especially when the obesity causes actual distress, is the menopausal woman apt to submit with faithfulness to the rigors of the reducing treatment.

The physical exercise most efficacious at this age is walking, systematic and prolonged, particularly if taken just after the principal meal.

Massage is rather useful, especially in cases with adipose localizations which so deform the feminine figure and because of their stubbornness constitute a worry to so many women. Under the most severe regimen the general weight may lessen notably and yet these localized adiposities will persist. On the other hand, they yield well to opotherapy and to massage.

"We do not speak ill of the masseuse," writes Elsie Lintner to her cousin, also menopausal, "since to her we owe the shapeliness of our hips."²¹

In these stubborn, climacteric obesities all the remaining physiologic remedies usually recommended find their maximum indication. Baths of all sorts are employed; of hot sand, of hot water, dry heat, vapor baths, and electric light baths which have proved very useful in several of my cases, as well as cool baths. The various electrotherapeutic methods have their value, such as sinusoidal electric baths, high frequency currents, continuous galvanic currents of high tension, static baths and douches and above all electric massage as employed by Bergonie. This constitutes an excellent auxiliary to the dietary regimen in obese patients who, for various reasons, cannot take the necessary active exercise. I have seen many obese women treated by this now popular means and I believe it truly useful in this variety of general adiposity. There are, nevertheless, cases which resist every treatment, not a gram of weight being lost in spite of effort and persistence; it doubtless then has been a matter of deep-rooted metabolic (endocrine) disturbances.

The employment of all these remedies is, in practice, very difficult. The patients consent to be subjected to them only during very short periods, because of the social and even economic difficulties which the length of time required imposes. For that reason in the cases in which the indication for reducing is fundamental, sojourns at sanatoria and health resorts are most useful, such places as Cestona, Vichy, Brides, Carlsbad, and Marienbad. In general I have observed excellent results.

In the treatment of the obesity of these women the opotherapeutic recourses have, as we have seen, a fundamental part. The most important and constantly applicable is whole ovarian ex-

²¹Michaelis: *Op. cit.*, note (3), page 200.

tract. I have often tried the influence on the weight, treating a hypogenital obese woman, menopausal or premenopausal, with total ovarian or lutein extracts alone without achieving the least reduction in weight, in spite of the persistence and the intensity of the doses employed. The same conclusion is deduced from the attempts of Carnot,²² Labbé²³ and others. But associated with the other means, opotherapeutic, dietetic or hygienic, it assists their reducing action. For this reason and for its beneficial influence on the general symptoms, it should always be employed.

Thyroid therapy, so useful in the endocrine obesities in general, finds precisely a contraindication in many cases of menopausal obesity on account of the frequency of the hyperthyroid reactions, spontaneous or provoked, at this age. Before deciding to give thyroid extract to a menopausal woman, and especially in the considerable doses which are required in order to obtain any appreciable reduction, we should carefully go into her symptomatology and determine her basal metabolic rate. We should omit thyroid medication in the presence of any one of the hyperthyroid symptoms, tachycardia, sweating, vasomotor irritability, goiter, excessive nervousness, etc., and above all, if the metabolic rate is higher than normal—+10. We should reserve this treatment, then, for those cases in which the obesity coincides with a syndrome which is *definitely hypothyroid*, with low basal metabolism.²⁴ And even in these cases strict vigilance must be maintained in order to suspend it at the first indications of thyroidism.

Hypophyseal therapy will be indicated in cases with localization of fat, especially if abdominal, with precocity of the hypogenital symptoms and in the presence of the other hypopituitary symptoms, such as somnolence, apathy and polyuria. It has the inconvenience of being an expensive product and its efficacy will be noted only on taking sufficiently energetic doses, 4, 6, or 8 tablets a day of the current preparations.

²²Carnot: Op. cit., note (19), page 338.

²³Labbé: Op. cit., note (4), page 239.

²⁴With Carrasco, I recently explained—op. cit., note (18), page 110—that the most practical value of the basal metabolic test is to enable the physician to decide the propriety or impropriety of employing thyroid, in spite of all clinical appearances.

In regard to the other various remedies employed in the treatment of obesity, we may take into account the following: (1) The iodides and the iodized preparations are most useful in cases with hypertension, but are to be used with greater prudence in climacteric women. Their use is contraindicated at once in women with goiter or in those who, without goiter, present suspicious hyperthyroid reactions. (2) Purgatives are useful in almost all cases of climacteric obesity, above all in the great number of patients who are constipated and hypertensive. Salts, especially the various saline laxatives, may be employed, or the laxative mineral waters as taken at Cestona, Carlsbad, Chatel-Guyon, Vals or Carabana. This useful action of laxatives is one of the chief benefits derived from the hydromineral "cures" before mentioned. (3) Other highly praised remedies in obesity are the alkalies, acids, *fucus vesiculosus*, and such metals as platinum and vanadium. They have a very limited scope. (4) Likewise the various pomades, soaps and other such remedies for external use are of little or no value.

Treatment of Adiposis, Lipomatosis and Angioneurotic Edema

The treatment of localized adiposes and lipomatoses is the same as that indicated for general obesity, massage and opotherapy being much stressed.

In cases of painful adiposity and in angioneurotic edema I am accustomed to prescribe combined hypophyseal thyroid and ovarian extracts, the latter very intensely. The iodides are apt to be useful, and also massage judiciously applied.

Climacteric Thinness; Its Treatment

The menopausal women who grow thin are apt to be, as I have already said, hyperthyroid in a great number of cases and therefore will require the usual treatment for hyperthyroidism. Their diet should consist of carbohydrates and fats, with a small amount of nitrogenous foods, and in certain cases even forced feeding may be guardedly employed. Physical and psychic re-

pose are essential. Ovarian extract and antithyroid medication such as serum and belladonna are of further value.

Hypophyseal thinness is, as we know, a true premature senile cachexia, not mere absence of fat.

Peculiarities in the Treatment of Climacteric Diabetes

The diabetes which presents itself in this age cannot be said to have a special treatment. The antidiabetic remedies, dietetic and pharmacologic, usual in ordinary cases and their complications, are applicable here in every way. However, it is proper for us to recall that diabetic states coinciding very precisely with the menopause, are related etiologically to emotional disturbances which follow a slow and benign course and which on examination offer us diverse and marked signs of the endocrine imbalance characteristic of the crisis. That is to say, the cases which we may designate as climacteric diabetes are not apt to require, in general, a diet very seriously deprived of carbohydrates and very rich in nitrogenous foods. This is an ideal easy to follow at present thanks to the help of insulin.

In cases of climacteric diabetes corresponding almost exactly to the hypertonic type, it will be found valuable to break the usual diet at more or less frequent intervals of a week or fifteen days by a day of stricter diet. Thus we may establish a "day of greens" or a "day of milk." Fast days or days of other exceptional diet of the same order may also be advised.

Something further may be said for the "fasting treatments" so praised by Allen and other American physicians and now universally accepted with more or less modification. My experience is rather extensive in this respect and I can state that, with rare exceptions, the Spanish diabetic will not submit to this regimen with the necessary faithfulness. On the other hand isolated days of fasting, such as I have advised for years, are very feasible and very useful, especially in cases not grave. These climacteric diabetics are precisely the ones which are most benefited by such a plan. One day in every fifteen, every twenty or every thirty, according to the intensity of the diabetic and general symptoms, the patient remains in bed, taking only water, a little tea, coffee

or alcohol. Generally this fasting is very well tolerated and the patient feels the benefit of its imposition.

Apart from insulin, ovarian therapy is useful where there are indications for it, as is antithyroid or hypotensive treatment as well.

Gout and Chronic Rheumatism

The states of gout and chronic rheumatism which are apt to coincide with the climacteric have no therapeutic peculiarities whatever. According to Freund²⁵ radium emanations are of value in these cases, stimulation of the languid ovarian function being attributed to them. "The proof of this," he says, "is that after a course of treatment by emanations, menstruation is apt to reappear." Ovarian therapy, like thyroid, has not afforded me any notable results, even though at times some result was appreciable in the many attempts which I have made in this direction. Even in cases in which particular disturbances appear clearly linked to the climacteric crisis through their chronology and symptoms, the best opotherapy theoretically indicated is apt to fail utterly in the presence of the deliberate stubbornness of these affections. The general state is apt to be benefited. For this reason and for the relative efficacy which at times is achieved in the articular symptoms themselves the best rule is to associate opotherapy with such other remedies as atophan and its like, iodine and analgesics and physiologic resources, radium emanations, baths and massage. Local or general mud baths as given at Archena or Dax are very useful.

Treatment of Gastric Disturbances. Hyperchlorhydria and Antithyroid Treatment

Among the symptoms of the digestive apparatus hyperchlorhydria and hypochlorhydria are treated as they are ordinarily, without stressing the severity of the diabetic regimen but emphasizing the general medication in regard to the clinical characteristics of the crisis in each case. For example, very frequently hyperchlorhydric women at this age present, as I have already said, a strong hyperthyroid reaction, which certainly acts in the

²⁵Freund: Op. cit., note (56), page 260.

production of the gastric disturbance. In this case, the anti-thyroid treatment, serum, belladonna, or general antithyroid regimen, is apt to alleviate considerably the gastric complaints resistant to the usual remedies. But none of this must be done without being certain, by a careful examination, of the absence of organic lesions like ulcer which would indicate altogether different treatment.

Flatulent Dyspepsia and Abdominal Massage

Flatulent dyspepsia so frequent in the climacteric, stubbornly resists treatment. In general a plain diet is proper and the remedies suggested by the endocrine, nervous and gastric study of each case. In Chapters XVII and XIX I explained the coincidence and probable pathogenic relations of this symptom with abdominal adiposity. The treatment there indicated to combat such adiposity appears to me to be most useful along with a general reducing regimen, especially massage and Swedish gymnastics. By such means I have obtained excellent results in many cases.

Pathogenic Treatment of Constipation and Diarrhea in the Climacteric

Apart from a suitable course of dietetic treatment climacteric constipation also requires opotherapy as a useful adjuvant. Wagner, and Alder cited by Foges²⁶ have described cases improved by ovarian therapy. I have observed several very illustrative ones and when the constipation coincides with hypothyroid symptoms, thyroid therapy alleviates the complaint at times in a most admirable way.

Climacteric diarrhea has as a characteristic its rebelliousness to the usual dietetic resources. Frequently such patients are subjected to a milk diet on which they almost always grow worse. Coarse foods act better on the digestive disturbance, but are not good in general because of their fattening and flatulent tendency. It is also a very important factor in the treatment of these conditions to procure for the patient a favorable emotional and

²⁶Foges: Keimdrüsen, in the book mentioned by Jauregg and Bayer.

psychic atmosphere. This is probably in part the secret of the indubitable efficacy of the hydromineral "baths" at Solares, Chatel-Guyon and like resorts. The chief benefits come from the physical and psychic repose enjoined by sojourns at these baths upon persons who have been living the fast and hectic life of society in the large cities.

Asthma and Genital Therapy

Asthma, the sole interesting manifestation which the respiratory tract offers us in the critical age, is a further indication for increasing ovarian therapy. It is precisely the repeated and specific efficacy of this medication in many cases of asthma (see page 302) that is one of the arguments on which I base the hypogenital hypothesis of its occurrence. It is clear that with ovarian extract must be combined the ordinary remedies, such as gome-nol, the iodides, caffein iodide, diet, climatology and balneotherapy. During the attack itself the usual abortive measures are injections of adrenalin, or of hypophyso-adrenalin. When the anaphylactic mechanism of the asthma is ascertained, which is not always the case, the disanaphylactic courses of treatment are in order. Regardless of the method employed ovarian therapy has its place.

Therapeutic Indications in the Disturbances of the Urinary Tract, and of the Skin, Eyes, Ears, etc.

All the disturbances of the urinary apparatus which can be related more or less directly to the climacteric crisis, can also be more or less directly influenced by genital therapy. Accordingly with respect to the patches of vesical congestion which some women repeatedly present at this age, Leopold-Levy told me that the good effect achieved by him in Pozzi's clinic with thyroid therapy in small doses harmonized with his conception of these congestive patches as due to a thyroid instability.

The symptomatology relating to affections of the skin, eyes and ears does not require any special therapeutic comment. Let me note only the undoubted beneficial influence of ovarian and thyroid therapy in certain eczemas, very resistant to local treat-

ment, which appear with some frequency in women of hypothyroid background whether the menopause is precocious or physiologic.²⁷

Surgical Menopause; Efficacy of Ovarian Therapy

Surgical menopause requires some further comment. Its fundamental treatment consists of ovarian therapy, preferably the whole extract, in vigorous and long-continued doses. I only point out that, at times, certain manifestations of the surgical climacteric, especially the suffocations, are profoundly resistant to treatment.

Treatment of the Masculine Climacteric. Testicular and Spermatic Therapy

The critical age of the man requires treatment corresponding to that detailed for the menopause of the woman, since, as I have demonstrated, he undergoes a somewhat similar endocrine crisis. The chief point of difference naturally is the employment of testicular extract instead of ovarian. Since the work of Brown-Sequard many and repeated tests have been made of the effects of testicular therapy and of the specific preparations based upon it.

But just as with extracts of the pancreas up to a short time ago, neither experimental nor clinical results demonstrate in testicular extracts a hormone comparable to that of other endocrine extracts prepared in the same way. This difference is very surprising if we take for comparison the homologous gland, the ovary. The unquestionable activity of partial or total extracts from the ovarian gland has not been reproduced in trials with the testicular gland. But there is no room for doubt that the testicle possesses a potent internal secretion, the complexity of its mode of action perhaps not being compatible with the crude preparation of its extracts which we use in our experimental studies and therapeutic tests. For myself, this failure is simply a question of technic which I hope, as with insulin, will be per-

²⁷To the bibliography on page 315, note 5—add: Alvarez Sainz de Aja; *Hechos positivos en endocrinología y dermatología*, Congreso de Sevilla, 1924.

fects at no distant date. Nevertheless Kylin and other writers report good results from the use of testicular therapy, even in symptoms as important as hypertension.

At times I have employed ovarian extract in men, with good results, as in Case 86. It appears that the so-called general hormones are common to both sexes. But even those hormones most specific may be, perhaps, susceptible to activation by crossed therapy, as is deduced from Nussbaum's work. He has produced experimentally reactivation of libido in male castrates by ovarian as well as by testicular grafts.

Let me recall, in closing, the old and now abandoned attempts of Poehl.²⁸ He assumed that extracts of the sperm [*espermina*] would contain the active endocrine substance of the testicular gland.

²⁸See the interesting book by Poehl, Fürts, Tarchanoff and Wachs: *Rationelle Organotherapie mit Berücksichtigung der Urosemilogie*. St. Petersburg, 1905.

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